이학석사학위논문

Rhodium-Catalyzed Oxygenative Addition of Alcohols and Amines to Terminal Alkynes for the Synthesis of Esters and Amides

말단 알카인의 알코올 및 아민과의 산화적 로듐촉매 첨가반응을 통한 에스터와 아마이드 합성

2013년 2월

서울대학교 대학원

화학부 유기화학 전공

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CONTENTS

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2012년 12월

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김인수의 석사학위논문을 인준함

2012년 12월

위 원 장 홍 순 혁

부위원장 이 철 범

위 원 최태림

ABSTRACT

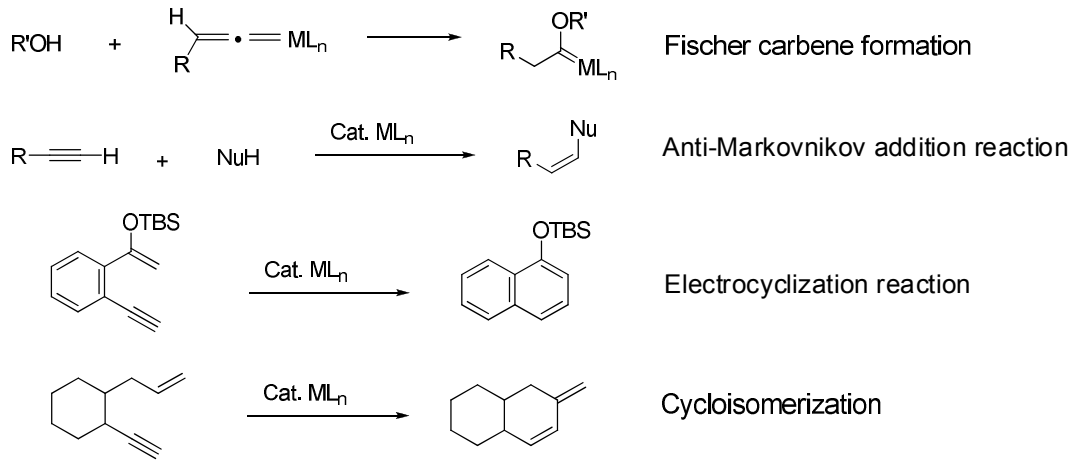
A rhodium-catalyzed reaction has been developed, in which terminal alkynes undergo an oxygenative addition with alcohols and amines to produce the corresponding esters and amides as the products. In this process, the rhodium vinylidene generated from a terminal alkyne is converted to a rhodium ketene complex by oxygen transfer from sulfoxides or *N*-oxides. Subsequently, the addition of nucleophiles such as alcohols and amines to the ketene complex gives esters and amides. Mechanistic studies suggest that the catalytic reaction involves the formation of a rhodium ketene complex via the oxidation of the metal-bound unsaturated carbene.

Keywords: Rhodium vinylidenes, Metallo ketene, Ester synthesis, Amide synthesis, Oxygenative addition

Student ID: 2011-20288

INTRODUCTION

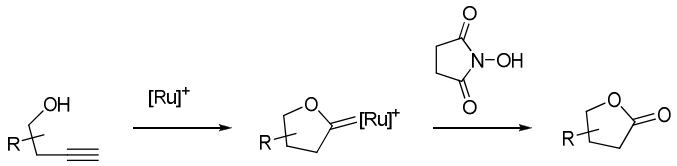
Because of the increasing importance of metal vinylidenes, there are many recent publications of metal vinylidene chemistry.[1] Traditionally, nucleophiles (such as alcohols) are added to metal vinylidenes in stoichiometric reactions to generate the corresponding Fischer carbene complexes. This mode of reactivity reflects the inherent electrophilicity of the vinylidene α-carbon atom. More recently, there has been a large number of publications that involve conversion of terminal alkynes into various products in which metal vinylidenes serve as catalytic species. Scheme 1 shows the some examples of metal vinylidene reactions.



Scheme 1. Reactions with metal vinylidenes

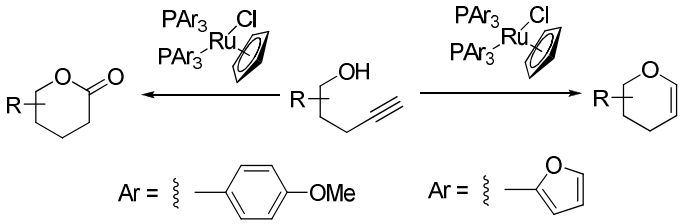
Trost and Rhee published ruthenium-catalyzed cycloisomerization-oxidation reactions.[2] They obtained the lactone moiety from homopropargyl alcohol using unconventional *N*-hydroxysuccinimide as an oxidant (Scheme 2). It was proposed that the reaction mechanism involves oxidation of the Fischer carbene complex. With

conventional oxidants (hydrogen peroxide, *m*-CPBA, pyridine *N*-oxide, DMSO), the reaction did not take place.



Scheme 2. Ruthenium catalyzed Fischer-carbene oxidation

In 2002, divergent ruthenium-catalyzed reactions of bis-homopropargylic alcohols were further reported, whereby a convenient access to either dihydropyrans or valerolactones was possible from the alkynes by using different phosphine ligands at the ruthenium center (Scheme 3). [3]

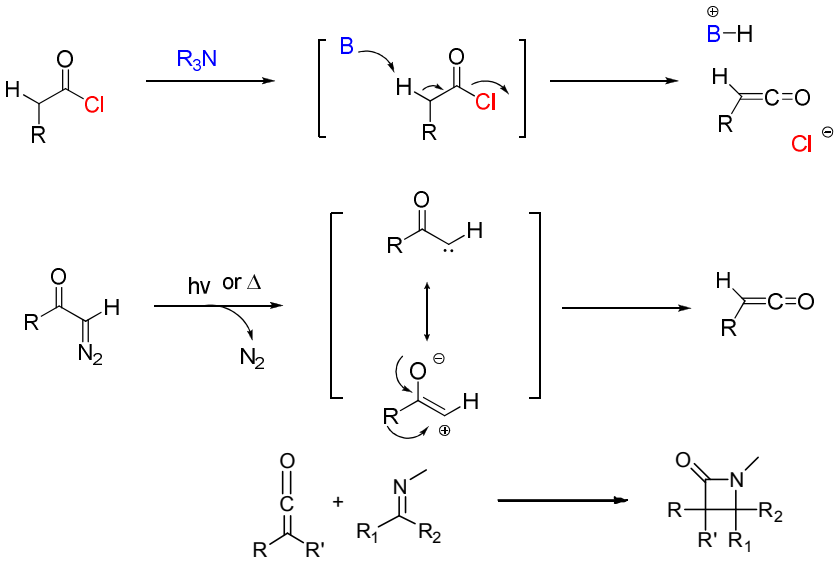


Scheme 3. Oxidative cyclization vs cycloisomerization of bis-homopropagyl alcohols

Simply, the change of ligand furnished different products. The use of the electron withdrawing phosphine ligand gave the dihydropyran product. On the other hand, an electron donating phosphine ligand such as trifurylphosphine delivered an oxidative cyclization product.

Ketenes[4] are highly useful intermediates in organic synthesis. The most common methods to access ketenes are base-assisted dehydrodehalogenation of acyl halides and Wolff rearrangement of α-diazo cabonyl compounds. There are many ketene-

cycloaddition reactions with aldehydes, alkenes, imines, among which the Staudinger [2+2] cycloaddition reaction of ketenes and imines to form β-lactams is one of the most important applications of ketene intermediates in organic synthesis (Scheme 4).

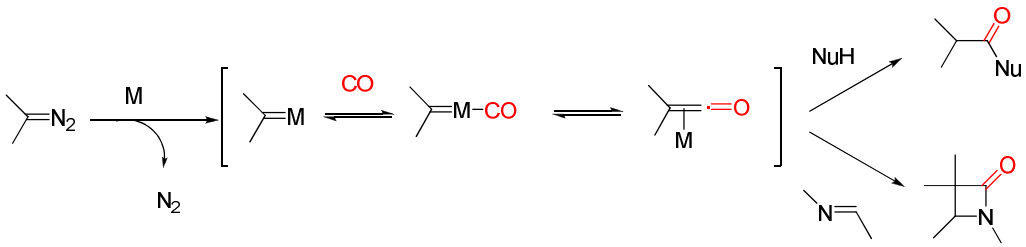


Scheme 4. General preparation of ketene and [2+2] Cycloaddition of ketene with imines

However, as reactive starting materials such as acyl halides or α-diazo carbonyl compounds are required for the generation of ketenes, their applications in the organic synthesis have been limited.

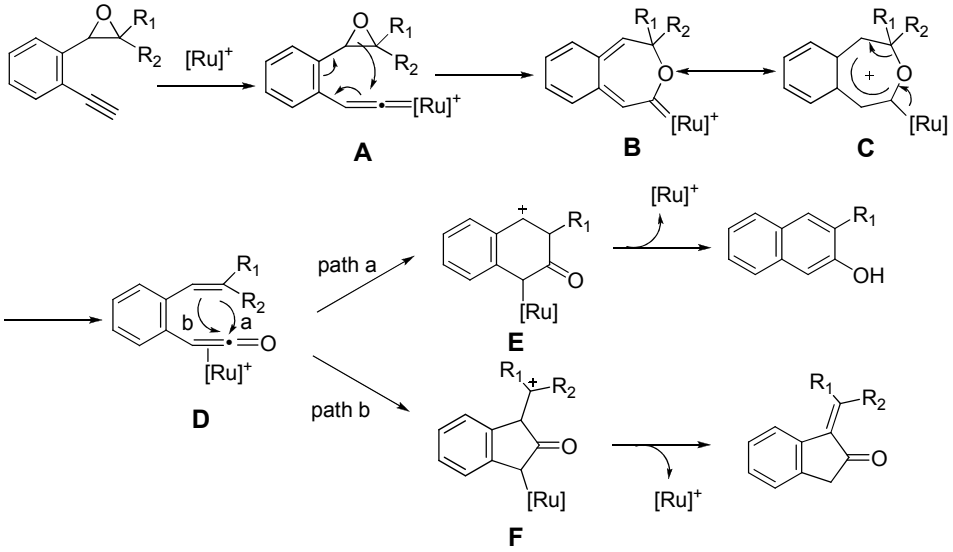
Catalytic carbonylation of metal carbene with CO so far has been only sporadically documented in the literature.[5] This type of reactions are limited by substrate scope and rigorous conditions such as high pressure of CO and high reaction temperatures. On the other hand, since diazo compounds are the most common precursors for the generation of metal carbenes, it would be natural to conceive the development of

transition metal-catalyzed carbonylation with diazo substrates (Scheme 5). In 2011, Jianbo Wang published Pd-catalyzed carbonylation of diazo compounds.[6] They obtained β-latam moiety in high yield using carbene equivalent and imine in mild conditions. The transition metal catalyzed carbonylation of metal carbene has been demonstrated the potential of such a reaction to be used as a general methodology for ketene generation.



Scheme 5. Catalytic carbonylation with Diazo compound

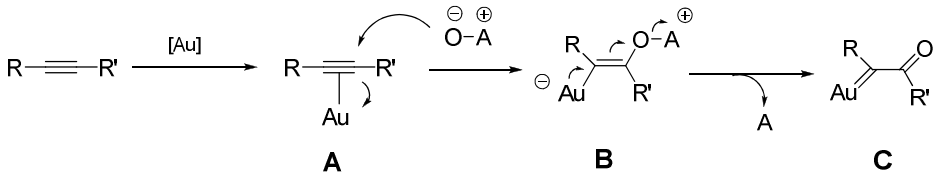
Rai-Shung Liu published formation of ketene intermediates via oxygen transfer from epoxides to terminal alkynes in 2004.[7] While 2-naphtols or 1-alkylidene-2-indanones was formed from (*o*-ethynyl)phenyl epoxides, a mechanism involving a metallo ketene intermediate was proposed (Scheme 6).



Scheme 6. Proposed mechanism by Rai-Shung Liu

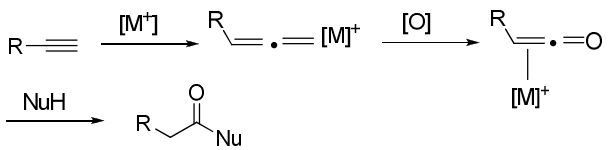
It has been proposed that the ruthenium catalyst first forms vinylidene-ruthenium species **A**, which is also supported by deuterium-labeling experiments. Intramolecular electrocyclization via attack of the epoxide oxygen to the α-carbon of the ruthenium vinylidene produces seven membered ether ring **B**, which is stabilized by extensive cationic delocalization **C**. The ruthenium-bound carbene **B** (and **C**) undergoes subsequent cleavage of the ether ring to give ruthenium-pi-ketene species **D**. In the case of disubstituted olefin, ruthenium-pi-ketene species **D** undergoes 6-endo-dig cyclization (path a) to form six-membered ketone species **E**, and ultimately gives naphthol. For trisubstituted olefin (R_2- alkyl), ruthenium-pi-ketene species **D** undergoes 5-endo-dig cyclization (path b) to give five-membered indanone species **F**, and finally gives 1-alkylidene-2-indanones.

The oxygenation of alkynes has been most frequently achieved by making use of gold catalysis. Gold catalysts are powerful soft Lewis acid for activating alkynes toward nucleophilic attack. Oxygen transfer oxidant react with the alkyne Au complex **A** via an addition-elimination process, donation an oxygen atom and leading to oxidative formation of α-gold carbenoid **C** (Scheme 7). This reaction concept first came from L. Zhang[8] and F. D. Toste,[9] respectively. This reaction type was significantly expanded by L. Zhang and Rai-Shung Liu,[10] most commonly using pyridine *N*-oxides and sulfoxides as oxidants.



Scheme 7. Synthesis of gold-catalyzed α-oxo gold carbenoid

With this background, we hypothesize the feasibility of following catalytic reaction (Scheme 8). Terminal alkynes and metal catalysts form the metal vinylidene species, and the oxygenative addition of this metal vinylidene using oxygen transfer oxidant gives metal ketene intermediates. Lastly, addition of nucleophiles to metal ketene intermediates provides to ester or amide products.



Scheme 8. Proposed reactions

RESULTS AND DISCCUSION

1. Intramolecular reactions

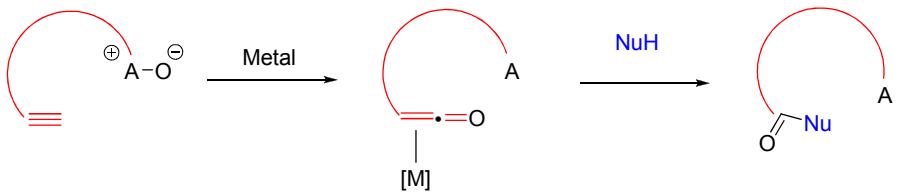
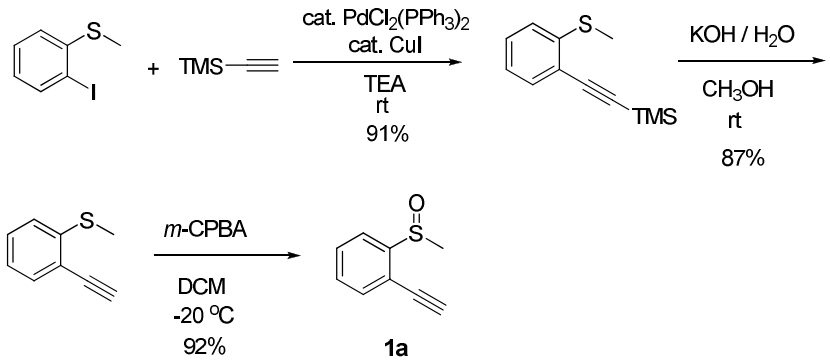


Figure 1. General scheme for intramolecular oxygen-transfer reactions

1.1. Sulfoxide substrates

1.1.1. Preparation of substrates



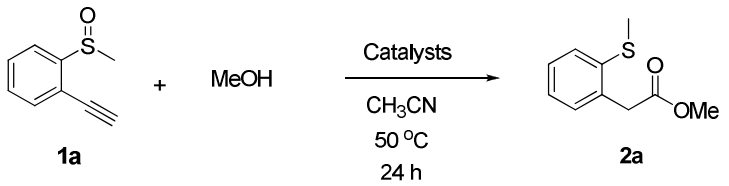
Scheme 9. Synthesis of substrates

In order to prepare the suitable model system having sulfoxide and alkyne groups within the same molecule, synthesized **1a** following the report of Larlock in 2008 (Scheme 9).[11] First, *o*-iodothioanisole was coupled with trimethylsilylacetylene using the Sonogashira reaction. Subsequently, deprotection of trimethylsilyl group

under basic conditions and oxidation of the sulfide with *m*-CPBA gave the desired sulfoxide.

1.1.2. Reaction discovery and optimization

Table 1. Screening of catalysts with sulfoxide substrates[a]



1a **2a**

Entry	Catalyst	Yield[b](%)
1	None	0
2	$CpRu(PPh_3)_2Cl$	5
3[c]	$[Ru(p\text{-}cymene)Cl]_2 + PPh_3$	4
4[c]	$CpRu(CH_3CN)_3PF_6 + PPh_3$	3
5	$TpRu(PPh_3)_2Cl$	4
6	$Rh(PPh_3)_3Cl$	51
7[c]	$[Rh(C_2H_4)_2Cl]_2 + PPh_3$	56
8[c]	$[Rh(COD)Cl]_2 + PPh_3$	59
9[c]	$[Rh(COD)Cl]_2 + P(4\text{-}OMe\text{-}C_6H_4)_3$	40
10[c]	$[Rh(COD)Cl]_2 + P(4\text{-}F\text{-}C_6H_4)_3$	76

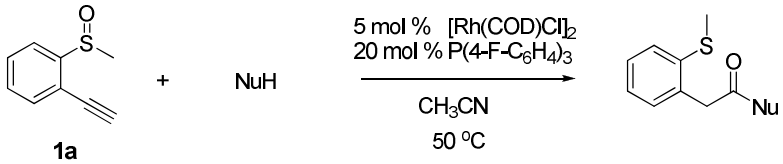
[a] All reactions were performed with 0.1 mmol of alkyne, 0.3 mmol of methyl alcohol, 5 mol % catalyst in 0.25 mL of CH_3CN at 50 °C for 24 h. [b] Determined by GC with 1,3,5-Trimethoxybenezene. as an internal standard. [c] 3 mol % catalyst and 12 mol % phosphine ligand were used.

Our initial efforts were focused on screening the metal catalysts known to be capable of mediating vinylidene catalysis for the addition of methyl alcohol substrate **1a** (Table 1). A series of ruthenium catalysts were first tested for the reaction, in which

alkyne **1a** was treated with 3 equivalents of methanol in acetonitrile in the presence of 5 mol % ruthenium complex at 50 ^{o}C. While no reaction took place in the absence of a ruthenium complex, the desired product **2a** could indeed be formed from the reactions using a series of ruthenium complexes, albeit in low yield. In particular, $TpRu(PPh_3)_2Cl$ the catalyst used by the Liu group for the formation of ketene intermediates via oxygen transfer reaction, also gave a low yield. To our delight, the use of Wilkinson's catalyst and $[Rh(COD)Cl]_2/PPh_3$ significatly improved the yield. While changing the ligand to $P(4\text{-}OMe\text{-}C_6H_4)_3$ lowered the yield slightly, the use of $P(4\text{-}F\text{-}C_6H_4)_3$ ligand gave the highest yield. Based on these results, the combination of 5 mol % $[Rh(COD)Cl]_2$ and 20 mol % $P(4\text{-}F\text{-}C_6H_4)_3$ was chosen as the standard conditions.

1.1.3. Nucleophile scope

Table 2. Reaction scope with various alcohols and amines[a]

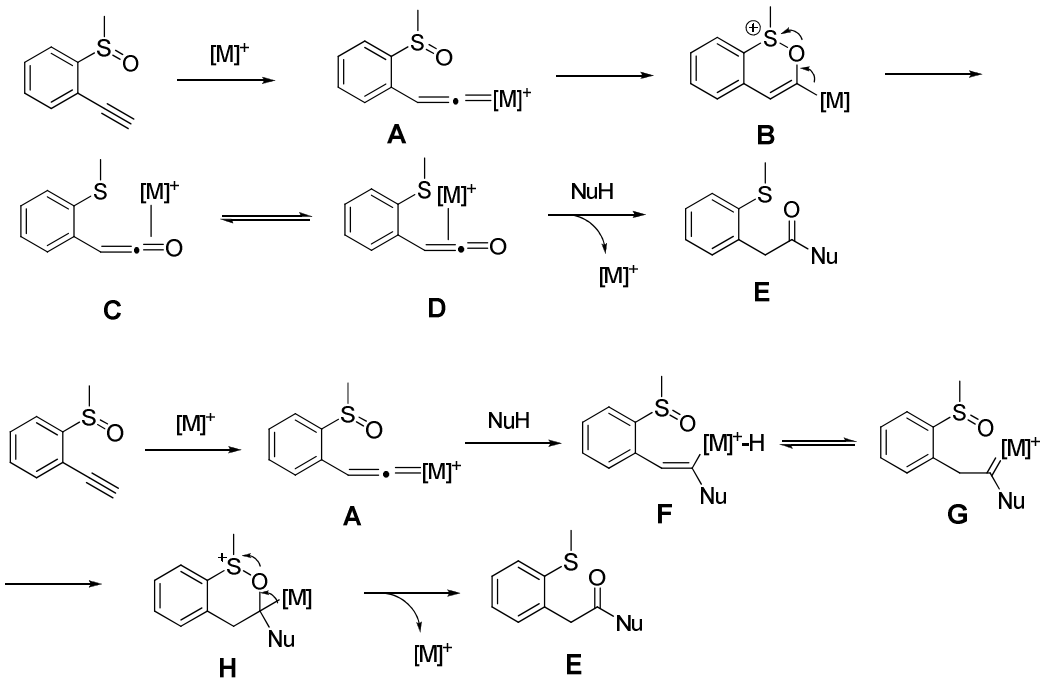


Entry	NuH	Yield[b](%)
1	EtOH	74 **(2b)**
2	Isopropyl alcohol	50 **(2c)**
3	Aniline	94 **(2d)**
4	*n*-Butylamine	61 **(2e)**
5	Morpholine	69 **(2f)**

[a] All reactions were performed with 0.5 mmol of alkyne, 2.5 mmol of alcohol and 0.6 mmol of amine in 1.25 mL of solvent at 50 °C for 12 h. [b] Isolated yield.

With the initial results, $[Rh(COD)Cl]_2/P(4\text{-}F\text{-}C_6H_4)_3$ catalysts system was considered to be the best catalyst for the reaction. To test the reaction scope (Table 2), other nucleophiles were also examined. Under the standard conditions, the reaction employing ethyl alcohol and isopropyl alcohol gave the ester product in moderate yields (**2b-2c**). This oxygenative addition reaction also worked well with amine nucleophiles. Both aromatic and aliphatic amines including primary and secondary amines participated in the reaction to give desired amide products in good yields (**2d-2f**).

1.1.4. Proposed reaction mechanism

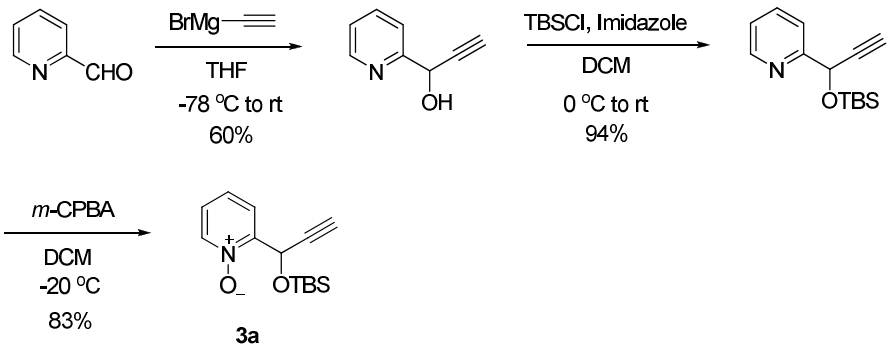


Scheme 10. Proposed reaction mechanism with sulfoxide substrates

Plausible mechanisms for this reaction are presented in Scheme 10. First of all, metal vinylidene **A** can be formed in the reaction condition. The oxygen of sulfoxide adds to the electrophilic α-carbon of metal vinylidene species **A** and the dissociation of metal-carbon bond furnishes metal-ketene intermediates **C** and **D**. Subsequent nucleophilic addition of the metal-ketene intermediates **C** gives an ester or an amide product **E**. Alternatively, the addition of nucleophiles to the metal vinylidene **A** to form the Fischer carbene complex **G**, which oxidized by sulfoxide to give ester or amide product **E** also can be proposed.

1.2. *N*-Oxide substrates

1.2.1. Preparation of substrates

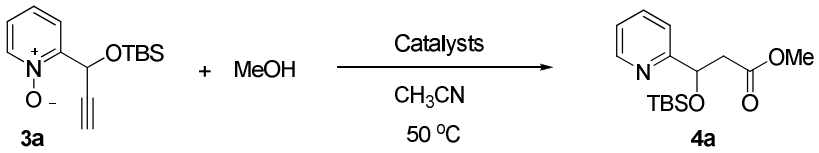


Scheme 11. Synthesis of substrates

Having established the oxygenative alkyne addition using an intramolecular sulfoxide group, we set out to examine the feasibility of *N*-oxides for the same reaction. Following the known procedure, the TBS protected alcohol was prepared from pyridine aldehyde.[12] The final *N*-oxidation was performed with *m*-CPBA to obtain **3a** (Scheme 11).

1.2.2. Reaction discovery and optimization

Table 3. Screening of catalysts with *N*-oxide substrates[a]



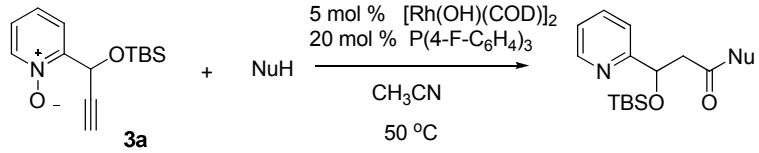
Entry	Catalyst	Yield[b](%)
1	$CpRu(PPh_3)_2Cl$	16
2	$Rh(PPh_3)_3Cl$	21
3[c]	$[Rh(COD)Cl]_2 + P(4\text{-}F\text{-}C_6H_4)_3$	35
4[c]	$[Rh(OH)(COD)]_2 + P(4\text{-}F\text{-}C_6H_4)_3$	46
5[c]	$[Rh(C_2H_4)(COD)]_2 + P(4\text{-}F\text{-}C_6H_4)_3$	28

[a] All reactions were performed with 0.1 mmol of alkyne, 0.5 mmol of methyl alcohol, 5 mol % catalyst in 0.25 mL of solvent at 50 °C for 24 h. [b] Determined by GC with 1,3,5-Trimethoxybenezene as an internal standard. [c] 3 mol % catalyst and 12 mol % phosphine ligand were used.

In a similar manner to the reactions of the sulfoxide, we screened metal catalysts. The reaction of *N*-oxide substrate (**3a**) with methyl alcohol was performed to explore the catalytic activities of various kinds of catalysts. As shown in Table 3, 3 mol % of $[Rh(OH)(COD)]_2$ and 12 mol % of PPh_3 was found to be the best reaction conditions for the formation of ester **4a**. However, the yield of ester product is relatively lower than the sulfoxide product.

1.2.3. Nucleophile scope

Table 4. Reaction scope with various alcohols and amines[a]

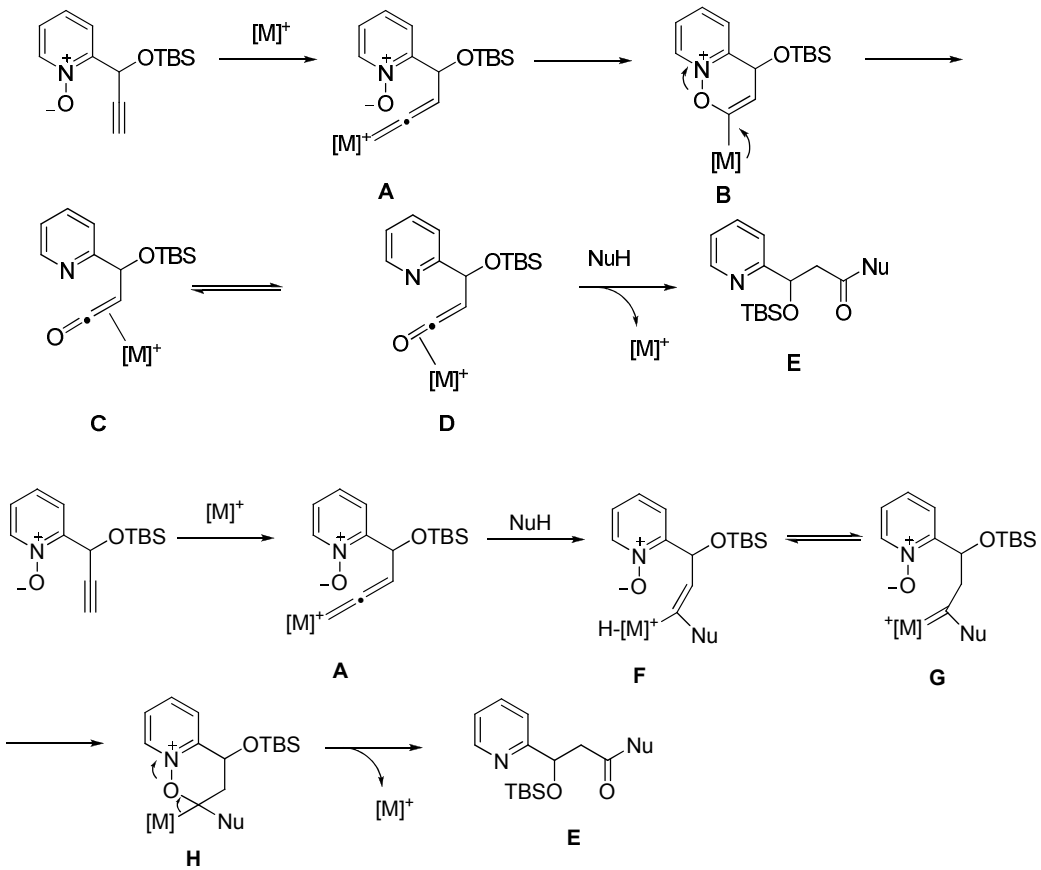


Entry	NuH	Yield[b](%)
1	EtOH	70 **(4b)**
2	Isopropyl alcohol	46 **(4c)**
3	Aniline	46 **(4d)**
4	*n*-Butylamine	77 **(4e)**
5	Morpholine	88 **(4f)**

[a] All reactions were performed with 0.2 mmol of alkyne, 1.0 mmol of alcohol and 0.24 mmol of amine, in 0.5 mL of solvent at 50 °C for 24 h. [b] Isolated yield.

The reaction scope of *N*-oxide **3a** was also tested. With ethyl alcohol and isopropyl alcohol as the nucleophiles, the reaction afforded the desired ester product in 70% and 46 %, respectively. Either alkyl or aryl amines also furnished the desired amide products (**4d-4f**) in good yields.

1.2.4. Proposed reaction mechanism



Scheme 12. Proposed reaction mechanism with *N*-oxide substrates

As depicted in Scheme 12, a mechanism similar to Scheme 10 is proposed for the *N*-oxide reaction.

2. Intermolecular reactions

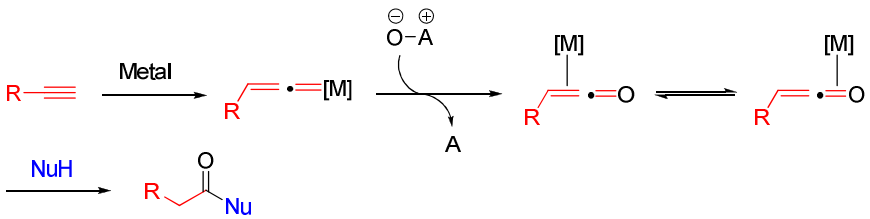
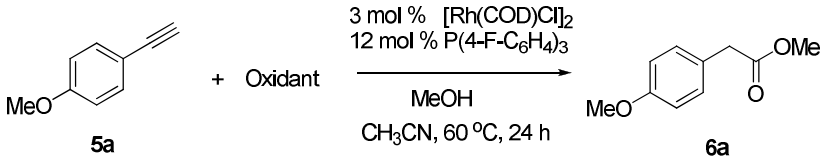
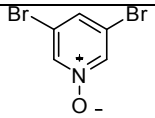
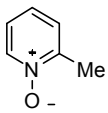
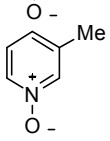
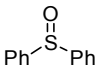
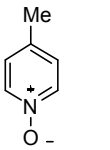
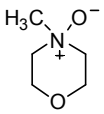
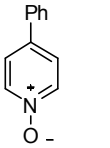
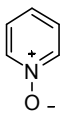
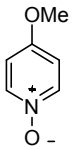
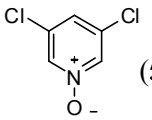
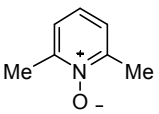


Figure 2. General scheme for intermolecular reactions

2.1. Reaction discovery and optimization

Table 5. Screening of oxidant with intermolecular reactions[a]

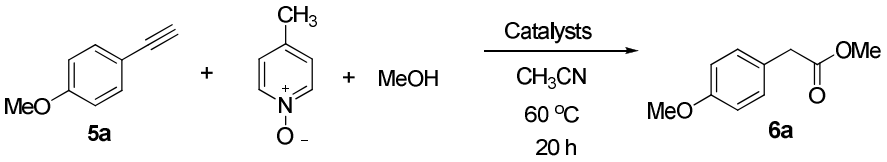


Entry	Oxidant		Yield[b](%)	Entry	Oxidant		Yield[b](%)
1	None	(**5b**)	0	8		(**5i**)	44
2		(**5c**)	0	9		(**5j**)	81
3		(**5d**)	0	10		(**5k**)	92
4		(**5e**)	0	11		(**5l**)	94
5		(**5f**)	0	12		(**5m**)	93
6		(**5g**)	87	13		(**5n**)	83
7		(**5h**)	54	14		(**5o**)	13

[a] All reactions were performed with 0.2 mmol of alkyne, 0.4 mmol of oxidant, 0.8 mmol of methyl alcohol in 0.4 mL of solvent at 60 °C for 24 h. [b] Determined by GC with 1,3,5-Trimethoxybenezene as an internal standard.

After we found the reaction using intramolecular sulfoxide and *N*-oxide substrates, our interest was focused on the intermolecular reaction. As the catalytic system using $[Rh(COD)Cl]_2/P(4\text{-}F\text{-}C_6H_4)_3$ proved to be the best conditions for the intramolecular reaction, our initial effort was to find the proper oxidant capable of transferring oxygen for the reaction. The reaction of 4-methoxyphenylacetylene (**5a**) with methyl alcohol was performed to examine the reactivity of *N*-oxides and sulfoxide oxidants. As shown in Table 5, a series of sp^2 hybridized nitrogen *N*-oxide gave the desired product. Among them, 4-picoline *N*-oxide (**5l**) was found to be the best oxidant for this reaction. A comparison of pyridine *N*-oxide, 2-picoline *N*-oxide (**5j**) and 2,6-lutidine (**5o**) *N*-oxide indicated that steric bulkyness of *N*-oxide hampers the reactions. When NMO (**5f**) was used as oxidant, we obtained the simple metal oxidation results. In contrast to pyridine *N*-oxide oxidant, sulfoxide oxidant proved to be much less efficient as oxygen transfer oxidant. 3,5-Dichloropyridine *N*-oxide (**5h**) and 3,5-Dibromopyridine *N*-oxide (**5i**) known to be good oxidants for the generation of the gold α-oxo carbenoid gave the product only in moderate yield.

Table 6. Screening of catalyst with intermolecular reactions[a]



Entry	Catalyst	Yield[b](%)
1	$CpRu(PPh_3)_2Cl$	44
2	$CpRu(dppm)_2Cl$	0
3[c]	$CpRu(CH_3CN)_3PF_6 + PPh_3$	26
4	$Rh(PPh_3)_3Cl$	80
5[c]	$[Rh(COD)Cl]_2 + PPh_3$	87
6[c]	$[Rh(COD)Cl]_2 + P(4\text{-}OMe\text{-}C_6H_4)_3$	82
7[c]	$[Rh(COD)Cl]_2 + P(4\text{-}F\text{-}C_6H_4)_3$	89
8[c]	$[Rh(C_2H_4)_2Cl]_2 + PPh_3$	60
9[c]	$[Rh(OH)(COD)]_2 + PPh_3$	30

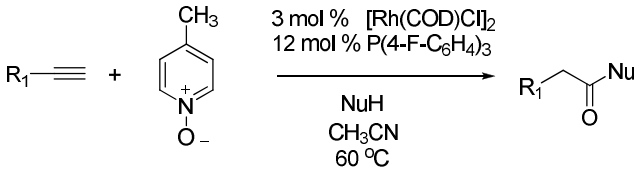
[a] All reactions were performed with 0.1 mmol of alkyne, 0.5 mmol of methyl alcohol, 0.15 mmol of 4-picoline *N*-oxide, 5 mol % catalyst in 0.25 mL of solvent at 60 °C for 20 h. [b] Determined by GC with 1,3,5-Trimethoxybenezene as an internal standard. [c] 3 mol % catalyst and 12 mol % phosphine ligand were used.

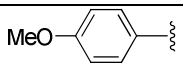
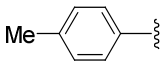
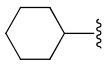
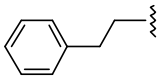
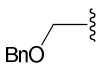
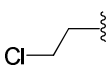
With 4-picoline *N*-oxide as the oxidant of choice, we next examined the catalysts. In these intermolecular reactions, some ruthenium complexes also displayed catalytic activity. For example, $CpRu(PPh_3)_2Cl$ afforded the desired product in 44% yield. Similar to the intramolecular reactions, $[Rh(COD)Cl]_2$/ $P(4\text{-}F\text{-}C_6H_4)_3$ once again turned out to be most efficient, while others such as $Rh(PPh_3)_3Cl$, $[Rh(C_2H_4)_2Cl]_2/PPh_3$, and $[Rh(OH)_2Cl]_2/PPh_3$ were less effective. In contrast to the intramolecular cases, ligand effects of $[Rh(COD)Cl]_2$ proved to be non-critical in

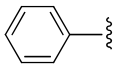
those intermolecular reactions (entries 5-7).

2.2. Substrate Scope

Table 7. Reaction scopes with various alkynes and nucleophiles[a]



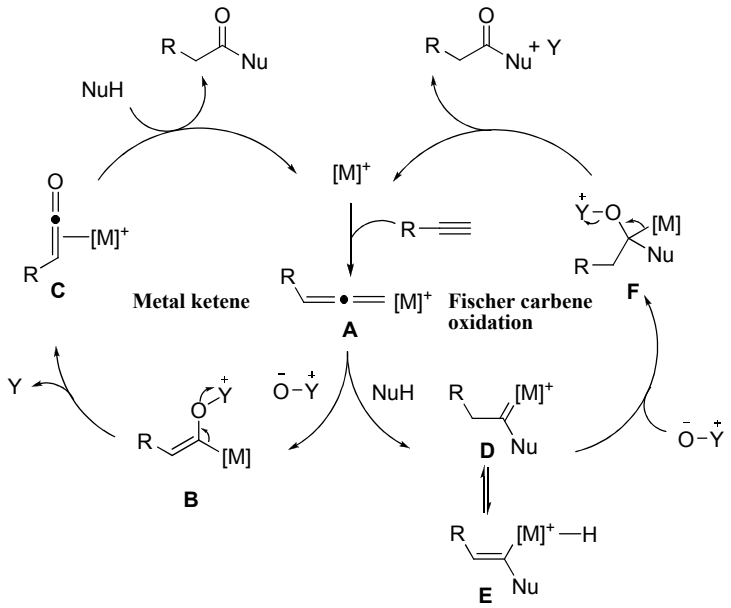
Entry	Alkyne (R_1)	NuH	Time (h)	Yield[b](%)
1		MeOH **(6a)**	2	95
2		EtOH **(6b)**	2	89
3		Phenol **(6c)**	2	71
4		Aniline **(6d)**	2	78
5		*N*-methylaniline **(6e)**	4	85
6		MeOH **(7a)**	2	89
7		Aniline **(7b)**	2	70
8[c]		MeOH **(8a)**	24	53
9		Aniline **(8b)**	24	36
10[c]		MeOH **(9a)**	4	82
11		Aniline **(9b)**	4	56
12[c]		MeOH **(10a)**	24	73
13		Aniline **(10b)**	24	66
14[c]		MeOH **(11a)**	19	75

15		Aniline **(11b)**	19	38
16[d]		MeOH **(12a)**	8	80
17[d]		Aniline **(12b)**	12	47

[a] All reactions were performed with 1.0 mmol of alkyne, 3.0 mmol of alcohol and 1.2 mmol of amine, 1.2 mmol of 4-picoline *N*-oxide in 2.0 mL of solvent at 60 °C. [b] Isolated yield. [c] 5.0 mmol of alcohol was used. [d] Reaction was carried out with 0.1 mmol of $[Rh(COD)Cl]_2$, 0.4 mmol of $P(4\text{-}F\text{-}C_6H_4)_3$, 10.0 mmol of alkyne, 12.0 mmol of 4-picoline *N*-oxide, 30.0 mmol of alcohol and 12.0 mmol of amine in 20.0 mL of solvent at 60 °C.

With the optimized conditions, the scope of these reaction was probed with a variety of alkynes using alcohol and arylamine nucleophiles. In general, when **5a** was employed, various alcohol and aniline afforded the corresponding esters or amides (**6a-6e**) in good yields. With 4-methylphenylacetylene, both methyl alcohol and aniline reacted well to provide the desired products. In addition, aliphatic alkynes such as cyclohexyl acetylene and 4-phenyl-1-butyne were also compatible with this reaction, providing the corresponding products (**8a-9b**). Benzyl-protected propargyl alcohol could also be used in the reaction to give the expected products (**10a-10b**). Using phenylacetylene, synthesis of esters or amides in gram scale has been achieved with 1 mol % of $[Rh(COD)Cl]_2$ and 4 mol % of $P(4\text{-}F\text{-}C_6H_4)_3$ (**12a-12b**).

2.3. Proposed Reaction Mechanism

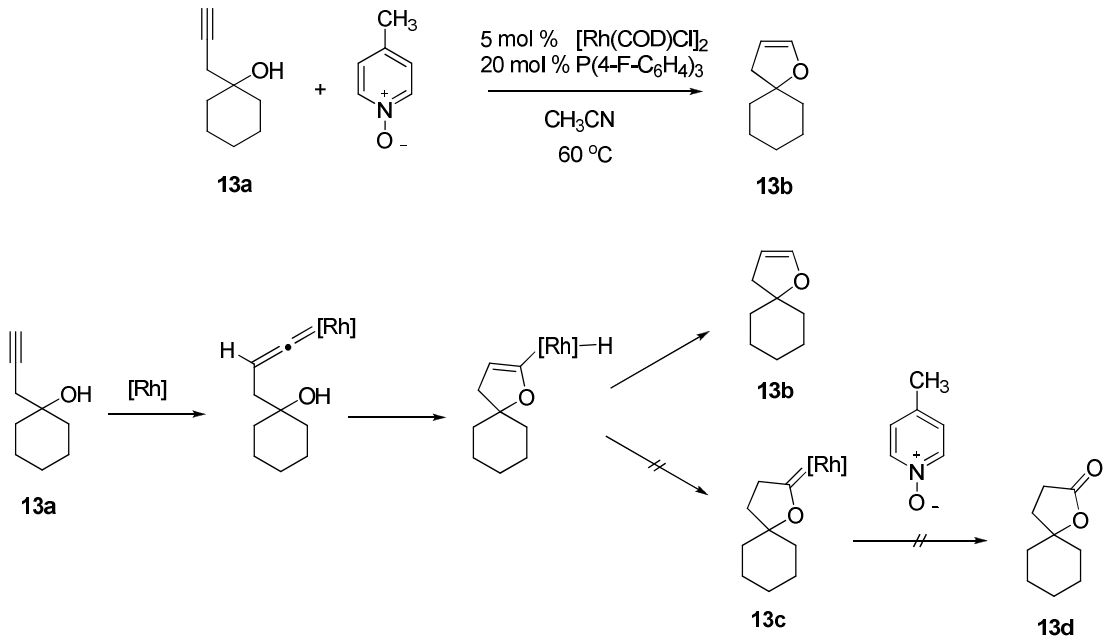


Scheme 13. Proposed reaction mechanism of intermolecular reactions

On the basis of the findings from our studies, the metal ketene formation mechanism and the Fischer carbene oxidation mechanism are proposed for the formation of esters or amides in Scheme 13. Metal vinylidene species **A** is formed by the reaction of the metal and a terminal alkyne. Then, the reaction of the metal vinylidene species with nucleophiles leads to the formation of Fischer carbene intermediate **D** that is in equilibrium with isomeric species **E**. Subsequently, Fischer carbene complex **D** is oxidized with an oxygen transfer oxidant to form intermediate **F**, which undergoes the carbon-metal bond dissociation to give the desired product. In contrast, if metal vinylidene species **A** reacts with the oxygen transfer oxidant to form intermediate **B**, the cabene-metal bond can be cleaved to give metal ketene complex **C**. And

addition of nucleophiles to the metal ketene affords the ester product.

In order to obtain clear mechanistic insight, we first tested rhodium-catalyzed oxidative cyclization reactions with homo-proparygyl alcohols substrate **13a** using 4-picoline *N*-oxide as an oxidant. If the reaction occurred through rhodium Fischer carbene oxidation mechanism, we obtained ɣ-butyrolactone product **13d**. However, we can obtain the cycloisomerization product **13b**. In 2003, Trost and Rhee published rhodium-catalyzed cycloisomerization reactions with homo- and bis-homopropargylic alcohols.[13] According to the paper, they also tried to find out oxidative cyclizaiton reaction with rhodium catalyst. However, all attempts to generate lactones using oxidant only led to cycloisomerization.



Scheme 14. Mechanistic studies

To the best of our knowledge, even though few examples about rhodium oxacarbenes complexes have been reported, [14] oxidation reaction of the rhodium oxacarbenes remains unknown. From this indirect evidence, we propose the reaction proceed through the rhodium ketene formation mechanism.

Conclusion

In summary, we have developed the first rhodium-catalyzed oxygenative addition reaction of terminal alkynes through the rhodium ketene intermediates. A mechanism for the formation of esters/amides was proposed on the basis of the results obtained by mechanistic studies. This method is highly useful for the synthesis of esters/amides. Now we are looking for the other reactions using this metal ketene intermediates.

EXPERIMENTAL SECTION

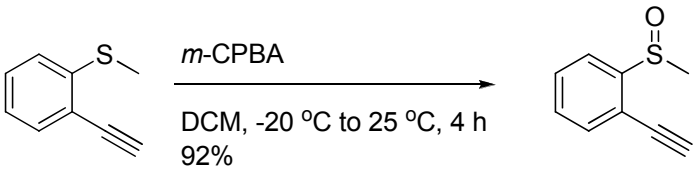
General information. NMR spectra were obtained on a Bruker DPX-300 (300 MHz), an Agilent 400-MR DD2 Magnetic Resonance System (400 MHz) and a Varian/Oxford As-500 (500 MHz) spectrophotometer. Chemical shift values were recorded as parts per million relative to tetramethylsilane as an internal standard unless otherwise indicated, and coupling constants in Hertz. The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were measured on a Thermo Scientific Nicolet 6700 spectrometer. High resolution mass spectra were recorded on a JEOL JMS-600W or a JEOL JMS-700 spectrometer using electron impact (EI) or chemical ionization (CI) method. CHI650B potentiostat, and gas chromatography data were obtained on a Hewlett Packard HP 6890 Series GC systems.

The progress of reaction was checked on thin layer chromatography (TLC) plates (Merck 5554 Kiesel gel 60 F254), and the spots were visualized under 254 nm UV light and/or charring after dipping the TLC plate into a vanillin solution (15.0 g of vanillin and 2.5 mL of concentrated sulfuric acid in 250 mL of ethanol), a $KMnO_4$ solution (3.0 g of $KMnO_4$, 20.0 g of K_2CO_3, and 5.0 mL of 5% NaOH solution in 300 mL of water), or a phosphomolybdic acid solution (250 mg phosphomolybdic acid in 50 mL ethanol). Column chromatography was performed on silica gel (Merck 9385 Kiesel gel 60) using hexanes-EtOAc (v/v). All solvents were obtained by passing through activated alumina columns of solvent purification systems from Glass

Contour.

Preparation of substrates

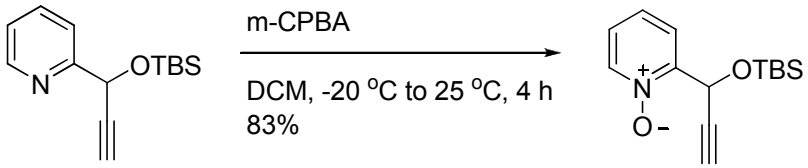
Sulfoxide substrates



1a

2-ethynylthioanisole was prepared according to the procedure described in the reference literature.[11] To a solution of 2-ethynylthioanisole (583 mg, 3.9 mmol) in CH_2Cl_2 (60 ml) was added *m*-chloroperbenzoic acid (678 mg, 3.9 mmol) in CH_2Cl_2 (20 ml) over a period of 30 min at 0 °C, and the mixture was stirred for 30 min before warming up to room temperature. After 4 h, the reaction mixture was filtered, and the filtrate was washed with saturated aqueous solution of sodium bicarbonate and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with water and dried over $MgSO_4$ and concentrated. Purification of the residue by flash column chromatography gave the desired product **1a** as pale yellow oil (596 mg, 3.63 mmol, 92% yield). R_f 0.17 (hexanes-EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.9 Hz, 1H), 7.62 (td, J = 7.9, 1.0 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.46 (td, J = 7.6, 1.1 Hz, 1H), 3.52 (s, 1H), 2.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.17, 133.53, 130.55, 130.39, 123.52, 118.21, 86.14, 78.81, 77.55, 77.23, 76.91, 42.35. IR (neat): ν_{max} 3284, 3207, 2100, 1462, 1071, 1039, 764 cm^{-1}. HRMS (EI) calcd. for C_9H_8OS (M^+): 255.1259, found 255.1259.

***N*-oxide substrates**



3a

2-(1-(tert-butyldimethylsilyloxy)prop-2-ynyl)pyridine was prepared according to the procedure described in the reference literature.[12] To a solution of 2-(1-(tert-butyldimethylsilyloxy)prop-2-ynyl)pyridine (3,540 mg, 14.3 mmol) in CH_2Cl_2 (23 ml) was added *m*-chloroperbenzoic acid (2,469 mg, 17.2 mmol) in CH_2Cl_2 (20 ml) over a period of 30 min at 0 °C, and the mixture was stirred for 30 min before warming up to room temperature. After 4 h, the reaction mixture was filtered, and the filtrate was washed with saturated aqueous solution of sodium bicarbonate and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with water and dried over Na_2SO_4 and concentrated. Purification of the residue by flash column chromatography gave the desired product **3a** as dark brown solid (3120 mg, 11.8 mmol, 83% yield). R_f 0.40 (CH_2Cl_2-MeOH, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 6.4 Hz, 1H), 7.70 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.27 – 7.21 (m, 1H), 5.99 (d, *J* = 1.8 Hz, 1H), 2.44 (d, *J* = 2.1 Hz, 1H), 0.95 (s, 9H), 0.25 (s, 3H), 0.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.94, 139.64, 126.22, 124.87, 123.57, 81.60, 77.55, 77.23, 76.91, 72.26, 59.45, 25.92, 18.42, -4.48, -4.96. IR (neat): ν_{max} 3304, 2955, 2929, 2887, 2857, 2112, 1646, 1431, 1247, 1082, 781 cm^{-1}. HRMS (CI) calcd. for $C_{14}H_{21}NO_2Si$ (M^++1): 264.1342, found 264.1420.

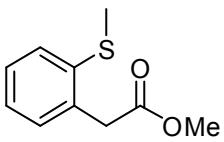
General procedure

General procedure for intramolecular reactions with sulfoixde substrates. To a vial equipped with a screw-cap were added a sulfoxide substrate **1a** (0.5 mmol), an alcohol (2.50 mmol) or amine (0.6 mmol), $[Rh(COD)Cl]_2$ (12.3 mg, 0.025 mmol, 5 mol %), $P(4\text{-}F\text{-}C_6H_4)_3$ (31.6 mg, 0.1 mmol, 20 mol %), and CH_3CN (1.25 mL). After sealing the vial with a screw-cap, the resulting yellow solution was heated at 50 °C. No special precautions were taken to exclude air or moisture, and the reaction was closely monitored by TLC analysis. Upon complete consumption of the starting alkyne (6 to 12 h), the reaction mixture was cooled to ambient temperature, and concentrated *in vacuo*. Purification by flash column chromatography afforded the ester or amide product in an analytically pure form.

General procedure for intramolecular reactions with *N*-oxide substrates. To a vial equipped with a screw-cap were added a *N*-oxide substrate **3a** (0.2 mmol), an alcohol (1.0 mmol) or amine (0.24 mmol), $[Rh(OH)(COD)]_2$ (4.56 mg, 0.01 mmol, 5 mol %), $P(4\text{-}F\text{-}C_6H_4)_3$ (12.65 mg, 0.04 mmol, 20 mol %), and CH_3CN (0.50 mL). After sealing the vial with a screw-cap, the resulting yellow solution was heated at 50 °C. No special precautions were taken to exclude air or moisture, and the reaction was closely monitored by TLC analysis. Upon complete consumption of the starting alkyne (12 to 24 h), the reaction mixture was cooled to ambient temperature, and concentrated *in vacuo*. Purification by flash column chromatography afforded the ester or amide product in an analytically pure form.

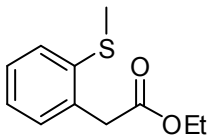
General procedure for intermolecular reactions. To a vial equipped with a screw-cap were added an alkyne substrates (1.0 mmol), an alcohol (3.0 mmol to 5.0 mmol) or amine (1.20 mmol), a picoline *N*-oxide (1.2 mmol), $[Rh(COD)Cl]_2$ (14.8 mg, 0.03 mmol, 3 mol %), $P(4\text{-}F\text{-}C_6H_4)_3$ (37.9 mg, 0.12 mmol, 12 mol %), and CH_3CN (2.0 mL). After sealing the vial with a screw-cap, the resulting yellow solution was heated at 60 °C. No special precautions were taken to exclude air or moisture, and the reaction was closely monitored by TLC analysis. Upon complete consumption of the starting alkyne (2 to 24 h), the reaction mixture was cooled to ambient temperature, and concentrated *in vacuo*. Purification by flash column chromatography afforded the ester or amide product in an analytically pure form.

Characterization data



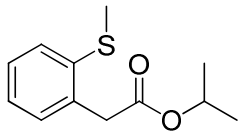
Methyl 2-(2-(methylthio)phenyl)acetate (2a)

^1H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.13 (d, J = 7.4 Hz, 1H), 7.06 (td, J = 7.5, 1.6 Hz, 1H), 3.71 (s, 2H), 3.62 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.87, 138.30, 133.25, 130.64, 128.26, 127.37, 125.76, 77.55, 77.23, 76.91, 52.34, 39.43, 16.81. IR (neat): ν_{max} 2950, 1978, 1738, 1435, 1161, 740 cm^{-1}. HRMS (EI) calcd. for $C_{10}H_{12}O_2S$ (M^+): 196.0558, found 196.0555.



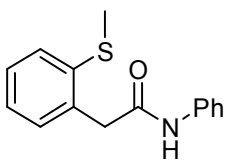
Ethyl 2-(2-(methylthio)phenyl)acetate (2b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.19 (m, 3H), 7.17 – 7.07 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 2H), 2.45 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.41, 138.29, 133.50, 130.59, 128.14, 127.47, 125.75, 77.55, 77.23, 76.91, 61.09, 39.63, 16.87, 14.40. IR (neat): ν_{max} 3061, 2983, 2924, 1735, 1590, 1159, 741 cm^{-1}. HRMS (EI) calcd. for $C_{11}H_{14}O_2S$ (M^+): 210.0715, found 210.0716.



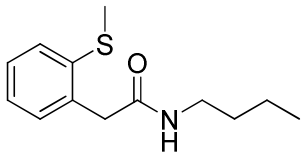
Isopropyl 2-(2-(methylthio)phenyl)acetate (2c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.10 (m, 4H), 5.13 – 4.97 (m, 1H), 3.75 (s, 2H), 2.45 (s, 3H), 1.27 – 1.21 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.97, 138.29, 133.76, 130.55, 128.07, 127.54, 125.76, 77.55, 77.43, 77.23, 76.91, 68.44, 39.94, 21.99, 16.94. IR (neat): ν_{max} 3061, 2981, 1979, 1732, 1164, 1107, 742 cm^{-1}. HRMS (EI) calcd. for $C_{12}H_{16}O_2S$ (M^+): 224.0871, found 224.0869.



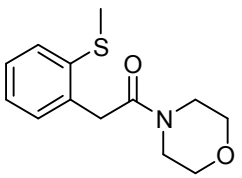
2-(2-(methylthio)phenyl)-*N*-phenylacetamide (2d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (br, 1H), 7.46 – 7.41 (m, 2H), 7.37 – 7.16 (m, 5H), 7.11 – 7.03 (m, 1H), 3.84 (s, 2H), 2.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.67, 138.07, 138.04, 133.30, 131.00, 129.09, 128.71, 127.18, 126.20, 124.46, 120.05, 77.55, 77.23, 76.91, 43.13, 16.47. IR (neat): ν_{max} 3303, 3058, 2920, 1739, 1664, 1544, 1441, 1175, 743cm^{-1}. HRMS (CI) calcd. for $C_{15}H_{15}NOS$ (M^++1): 258.0874, found 258.0953.



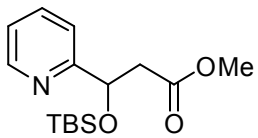
***N*-butyl-2-(2-(methylthio)phenyl)acetamide (2e)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 3H), 7.20 – 7.12 (m, 1H), 5.59 (br, 1H), 3.68 (s, 2H), 3.34 – 3.06 (m, 2H), 2.49 (s, 3H), 1.45 – 1.34 (m, 2H), 1.30 – 1.23 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.31, 138.26, 133.72, 130.88, 128.38, 126.80, 125.87, 77.55, 77.23, 76.91, 42.08, 39.56, 31.71, 20.14, 16.29, 13.88. IR (neat): ν_{max} 3293, 2958, 2929, 1748, 1646, 1550, 1250, 739 cm^{-1}. HRMS (CI) calcd. for $C_{13}H_{19}NOS$ (M^++1): 251.1278, found 251.1283.



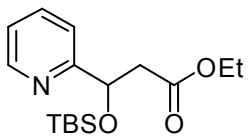
2-(2-(methylthio)phenyl)-1-morpholinoethanone (2f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 3H), 7.19 – 7.11 (m, 1H), 3.79 (s, 2H), 3.67 (s, 4H), 3.55 (s, 2H), 3.42 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.63, 137.18, 133.71, 129.29, 127.92, 126.74, 125.75, 77.55, 77.23, 76.91, 67.04, 66.76, 46.60, 42.42, 38.13, 16.41. IR (neat): ν_{max} 3058, 2965, 2920, 2855, 1647, 1436, 1115, 745 cm^{-1}. HRMS (CI) calcd. for $C_{13}H_{17}NO_2S$ (M^++1): 252.0980, found 252.1058.



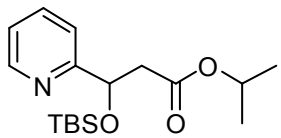
Methyl 3-(tert-butyldimethylsilyloxy)-3-(pyridin-2-yl)propanoate (4a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 7.69 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.20 – 7.13 (m, 1H), 5.27 (dd, *J* = 8.7, 4.0 Hz, 1H), 3.68 (s, 3H), 2.83 (dd, *J* = 14.6, 4.0 Hz, 1H), 2.69 (ddd, *J* = 17.1, 9.9, 4.6 Hz, 1H), 0.89 (s, 9H), 0.07 (s, 4H), -0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.55, 163.33, 148.89, 136.81, 122.47, 120.34, 77.55, 77.23, 76.91, 73.36, 51.72, 44.57, 25.92, 18.28, -4.58, -5.03. IR (neat): ν_{max} 2956, 2929, 2897, 2856, 1744, 1712, 1646, 1434, 1253, 1084, 839, 738cm^{-1}. HRMS (CI) calcd. for $C_{15}H_{25}NO_3Si$ (M^++1): 296.1604, found 296.1682.



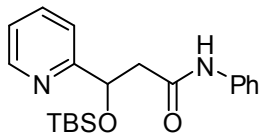
Ethyl 3-(tert-butyldimethylsilyloxy)-3-(pyridin-2-yl)propanoate (4b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.1 Hz, 1H), 7.69 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.16 (dd, *J* = 6.5, 5.0 Hz, 1H), 5.27 (dd, *J* = 8.6, 4.0 Hz, 1H), 4.22 – 4.04 (m, 2H), 2.81 (dd, *J* = 14.6, 4.0 Hz, 1H), 2.69 (dd, *J* = 14.6, 8.6 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), -0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.14, 163.42, 148.86, 136.79, 122.44, 120.42, 77.55, 77.23, 76.91, 73.38, 60.64, 44.80, 25.94, 18.30, 14.40, -4.56, -4.99. IR (neat): ν_{max} 2956, 2929, 2889, 2857, 1748, 1646, 1433, 1253, 738 cm^{-1}. HRMS (CI) calcd. for $C_{16}H_{27}NO_3Si$ (M^++1): 310.1760, found 310.1838.



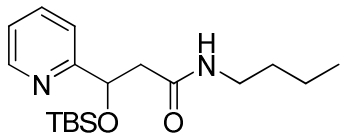
Isopropyl 3-(tert-butyldimethylsilyloxy)-3-(pyridin-2-yl)propanoate (4c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.19 – 7.14 (m, 1H), 5.26 (dd, *J* = 8.1, 4.2 Hz, 1H), 5.04 – 4.94 (m, 1H), 2.81 – 2.74 (m, 1H), 2.73 – 2.65 (m, 1H), 1.21 (t, *J* = 6.0 Hz, 7H), 0.92 – 0.88 (m, 9H), 0.11 – 0.07 (m, 3H), -0.06 – -0.10 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.63, 163.47, 148.81, 136.72, 122.38, 120.48, 77.55, 77.23, 76.91, 73.28, 68.00, 44.92, 25.96, 22.10, 22.03, 18.30, -4.57, -4.91.



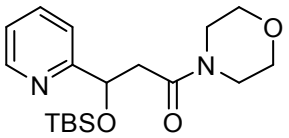
3-(tert-butyldimethylsilyloxy)-*N*-phenyl-3-(pyridin-2-yl)propanamide (4d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 – 8.52 (m, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 3H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.19 (dd, *J* = 7.2, 5.1 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 5.26 (t, *J* = 5.4 Hz, 1H), 2.96 (dd, *J* = 14.7, 4.8 Hz, 1H), 2.86 (dd, *J* = 14.6, 6.0 Hz, 1H), 0.93 (s, 9H), 0.11 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.69, 162.45, 149.04, 138.41, 137.16, 129.15, 124.13, 122.78, 120.42, 119.81, 77.55, 77.23, 76.91, 73.16, 47.07, 26.03, 18.35, -4.70, -4.80. IR (neat): ν_{max} 2956, 2929, 2889, 2858, 1712, 1646, 1434, 1266, 1084, 739 cm^{-1}. HRMS (CI) calcd. for $C_{20}H_{27}NO_3Si$ (M^++1): 357.1920, found 357.1998.



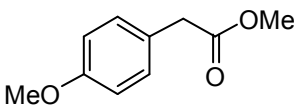
***N*-butyl-3-(tert-butyldimethylsilyloxy)-3-(pyridin-2-yl)propanamide (4e)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 4.7, 0.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.6 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.08 (m, 1H), 6.24 (br, 1H), 5.13 (dd, *J* = 6.3, 5.0 Hz, 1H), 3.26 – 3.05 (m, 2H), 2.72 – 2.58 (m, 2H), 1.37 (tq, *J* = 14.3, 7.1 Hz, 2H), 1.32 – 1.18 (m, 2H), 0.86 (s, 9H), 0.03 (s, 3H), -0.11 (s, 3H). IR (neat): ν_{max} 3301, 3067, 2957, 2929, 2857, 1645, 1555, 1471, 1257, 1107, 1081, 950, 831, 779, 741 cm^{-1}. HRMS (EI) calcd. for $C_{18}H_{32}N_2O_2Si$ (M^+): 336.2233, found 336.2230.



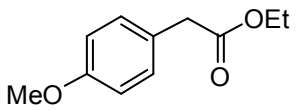
3-(tert-butyldimethylsilyloxy)-*1*-morpholino-3-(pyridin-2-yl)propan-1-one (4f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.72 – 7.66 (m, 1H), 7.47 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.20 – 7.16 (m, 1H), 5.32 (t, *J* = 6.3 Hz, 1H), 3.71 – 3.47 (m, 10H), 2.84 – 2.81 (m, 2H), 0.90 – 0.85 (m, 10H), 0.08 – 0.04 (m, 3H), -0.03 – -0.07 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.41, 163.23, 149.13, 136.76, 122.54, 120.90, 77.55, 77.23, 76.91, 73.77, 67.01, 66.83, 46.64, 42.16, 42.11, 26.02, 18.35, -4.66, -4.68.



Methyl 2-(4-methoxyphenyl)acetate (6a)[15]

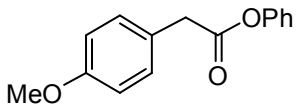
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 3.68 (s, 3H), 3.57 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 172.56, 158.91, 130.47, 126.26, 114.22, 77.55, 77.23, 76.91, 55.47, 52.20, 40.50.



Ethyl 2-(4-methoxyphenyl)acetate (6b)[16]

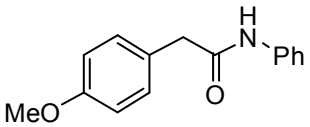
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.54 (s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR

(100 MHz, $CDCl_3$) δ 172.11, 158.84, 130.43, 126.43, 114.15, 77.55, 77.23, 76.91, 60.95, 55.43, 40.70, 14.38.



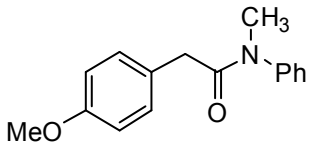
Phenyl 2-(4-methoxyphenyl)acetate (6c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 4H), 7.20 (dd, *J* = 14.0, 6.6 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.78 (d, *J* = 2.6 Hz, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.47, 159.05, 150.95, 130.52, 129.53, 125.97, 125.68, 121.63, 114.31, 77.55, 77.23, 76.91, 55.43, 40.71. IR (neat): ν_{max} 2957, 2836, 1753, 1611, 1591, 1513, 1492, 1250, 1182, 1125, 1033, 923, 739 cm^{-1}. HRMS (EI) calcd. for $C_{15}H_{14}O_3$ (M^+): 242.0943, found 242.0945.



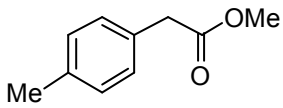
2-(4-methoxyphenyl)-*N*-phenylacetamide (6d)[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.8 Hz, 2H), 7.26 (dd, *J* = 14.9, 8.4 Hz, 4H), 7.14 (br, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 3.82 (s, 3H), 3.67 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.71, 159.29, 137.83, 130.89, 129.12, 126.50, 124.59, 119.94, 114.85, 77.55, 77.23, 76.91, 55.52, 44.15.



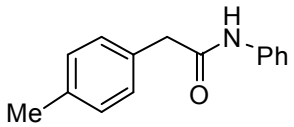
2-(4-methoxyphenyl)-*N*-methyl-*N*-phenylacetamide (6e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dq, *J* = 14.3, 7.1 Hz, 3H), 7.12 (d, *J* = 7.2 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 3.77 (s, 3H), 3.39 (s, 2H), 3.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.55, 158.53, 144.27, 130.24, 129.87, 128.08, 127.85, 113.96, 77.55, 77.23, 76.91, 55.45, 40.20, 37.79. IR (neat): ν_{max} 3052, 2956, 2834, 1751, 1655, 1595, 1512, 1377, 1248, 1178, 1122, 1034, 739 cm^{-1}. HRMS (EI) calcd. for $C_{16}H_{17}NO_2$ (M^+): 255.1259, found 255.1255.



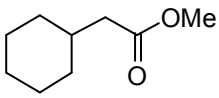
Methyl 2-p-tolylacetate (7a)[17]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (q, *J* = 8.1 Hz, 4H), 3.68 (s, 3H), 3.59 (s, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.45, 136.96, 131.14, 129.50, 129.32, 77.55, 77.23, 76.91, 52.23, 41.02, 21.30.



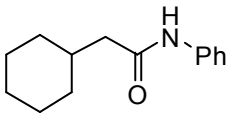
***N*-phenyl-2-p-tolylacetamide (7b)**[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.8 Hz, 3H), 7.31 – 7.21 (m, 2H), 7.22 – 7.14 (m, 4H), 7.06 (dd, *J* = 10.7, 4.1 Hz, 1H), 3.66 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.70, 137.92, 137.46, 131.56, 130.02, 129.55, 129.04, 124.52, 120.05, 77.55, 77.23, 76.91, 44.50, 21.28.



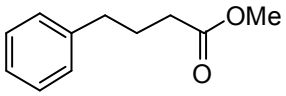
Methyl 2-cyclohexylacetate (8a)[18]

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.19 (d, *J* = 7.0 Hz, 2H), 1.86 – 1.60 (m, 6H), 1.35 – 1.20 (m, 2H), 1.20 – 1.07 (m, 1H), 1.03 – 0.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.82, 77.55, 77.23, 76.91, 51.55, 42.20, 35.10, 33.25, 26.35, 26.24.



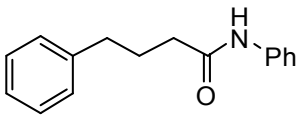
2-cyclohexyl-*N*-phenylacetamide (8b)[19]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (t, *J* = 9.5 Hz, 3H), 7.29 (dd, *J* = 15.2, 7.2 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 2.21 (d, *J* = 7.1 Hz, 2H), 1.96 – 1.61 (m, 6H), 1.34 – 1.21 (m, 2H), 1.21 – 1.08 (m, 1H), 1.06 – 0.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.19, 138.20, 129.14, 124.37, 120.10, 77.58, 77.26, 76.94, 46.09, 35.73, 33.36, 26.39, 26.27.



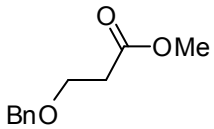
Methyl 4-phenylbutanoate (9a)[20]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.4 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 3H), 3.65 (s, 3H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.32 (t, *J* = 7.5 Hz, 2H), 2.01 – 1.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.08, 141.52, 128.64, 128.54, 126.14, 77.55, 77.23, 76.91, 51.66, 35.28, 33.54, 26.65.



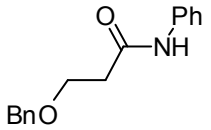
***N*,4-diphenylbutanamide (9b)**[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.9 Hz, 2H), 7.29 (dd, *J* = 13.7, 7.2 Hz, 4H), 7.19 (t, *J* = 6.8 Hz, 4H), 7.09 (t, *J* = 7.4 Hz, 1H), 2.70 (t, *J* = 7.4 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.13 – 1.98 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.14, 141.53, 138.06, 129.19, 128.72, 128.65, 126.25, 124.42, 119.97, 77.55, 77.23, 76.91, 36.96, 35.25, 27.04.



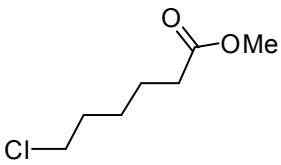
Methyl 3-(benzyloxy)propanoate (10a)[21]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 5H), 4.53 (s, 2H), 3.74 (t, *J* = 6.4 Hz, 2H), 3.69 (s, 3H), 2.62 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.18, 138.24, 128.55, 127.84, 127.83, 77.55, 77.23, 76.91, 73.28, 65.74, 51.84, 35.15.



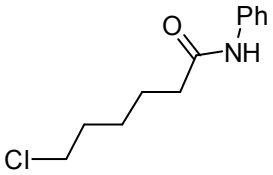
3-(benzyloxy)-*N*-phenylpropanamide (10b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (br, 1H), 7.42 (t, *J* = 8.6 Hz, 2H), 7.40 – 7.22 (m, 7H), 7.08 (t, *J* = 7.4 Hz, 1H), 4.60 (s, 2H), 3.84 (t, *J* = 5.6 Hz, 2H), 2.67 (t, *J* = 5.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.91, 138.28, 137.57, 129.14, 128.86, 128.34, 128.13, 124.24, 119.94, 77.55, 77.23, 76.91, 73.78, 66.61, 38.39. IR (neat): ν_{max} 3316, 3059, 2869, 1749, 1712, 1663, 1599, 1443, 1363, 1310, 1102, 755, 697cm^{-1}. HRMS (EI) calcd. for $C_{16}H_{17}NO_2$ (M^+): 255.1259, found 255.1259.



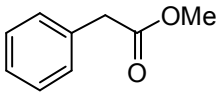
Methyl 5-chlorohexanoate (11a)[22]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.34 (t, *J* = 7.4 Hz, 2H), 1.85 – 1.75 (m, 2H), 1.72 – 1.60 (m, 2H), 1.54 – 1.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.13, 77.55, 77.23, 76.91, 51.75, 44.98, 34.05, 32.42, 26.58, 24.39.



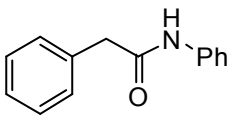
6-chloro-N-phenylhexanamide (11b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.9 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 3H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.37 (t, *J* = 7.4 Hz, 2H), 1.89 – 1.69 (m, 4H), 1.59 – 1.46 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.17, 138.04, 129.20, 124.47, 120.00, 77.55, 77.23, 76.91, 45.05, 37.66, 32.48, 26.67, 24.96.



Methyl 2-phenylacetate (12a)[15]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 1H), 3.70 (d, *J* = 1.8 Hz, 1H), 3.63 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.23, 134.17, 129.45, 128.78, 127.31, 77.55, 77.23, 76.91, 52.25, 41.40.



***N*,2-diphenylacetamide (12b)**[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.21 (m, 9H), 7.07 (t, *J* = 7.4 Hz, 1H), 3.69 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.44, 137.85, 134.67, 129.65, 129.31, 129.07, 127.75, 124.59, 120.07, 77.55, 77.23, 76.91, 44.89.

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국문 초록

로듐 촉매를 이용하여 말단 알카인에 대한 알코올과 아민의 산화적 첨가 반응을 통하여 에스터와 아마이드 합성 반응을 개발하였다. 이 반응에서 말단 알카인으로부터 생성된 로듐 vinylidene은 sulfoxide 또는 *N*-oxides로부터 산소 전달 반응을 통하여 로듐 키틴 착화물로 바뀌게 된다. 다음의 알코올이나 아민과 같은 친핵체가 키틴 착화합물과 첨가 반응하여 에스터나 아마이드 화합물을 주게 된다. 반응경로 연구를 통하여 금속에 붙어있는 불포화 카빈의 옥시데이션 반응을 통하여 로듐 키틴 착화합물이 생성되는 과정을 포함하는 촉매 반응이 제안되었다.

주요어: 로듐 vinylidene, 금속 키틴, 에스터 합성, 아마이드 합성, 산소 첨가반응

학번: 2011-20288

감사의 글

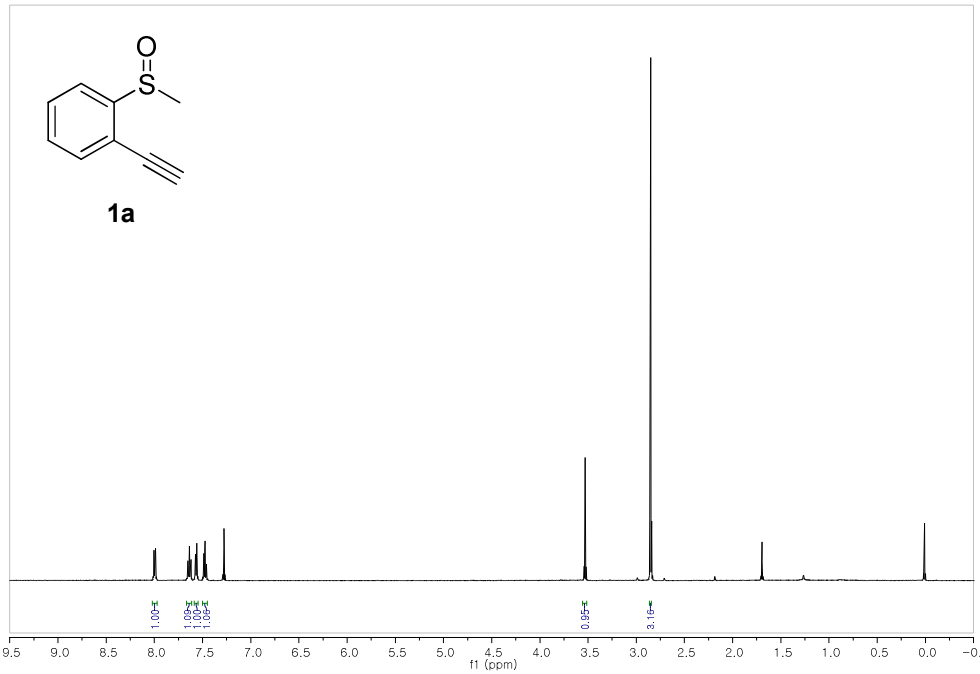
실험실에 들어온게 엊그제 같은데 벌써 2년의 시간이 흘러 석사학위 졸업논문을 쓰게 되니 감회가 새롭습니다. 다음 학기부터 박사과정을 시작하게 되어 실험실을 떠나는 것은 아니지만 이 기회를 통해 그 동안 실험실 생활을 하며 도움을 주신 분들에게 감사의 인사를 전하고자 합니다. 가장 먼저 학위 과정 동안 지도해 주신 이철범 교수님께 감사를 드립니다. 학위 과정 동안 연구나 생활에 불편함이 없는 환경을 제공해 주시고 학자로서의 마음가짐이나 연구자세 등을 알려주셔서 감사합니다. 또한 논문 심사를 위해 귀한 시간을 내어주신 홍순혁 교수님, 최태림 교수님, 그리고 제가 유기 화학을 할 수 있게 이끌어 주신 고려대 정낙철 교수님께 감사의 말씀을 드리고 싶습니다.

실험실 동기면서 후드를 1년 6개월 가량 같이 쓰면서 동고동락했던 재우, 쓸쓸했던 1번 라인의 말벗이 되어주었던 동석, 승주, 진, 장난 잘 받아준 은혜, 호윤, 성현, 성미, 논문 준비하면서 큰 도움을 준 혜진, 같은 프로젝트 하는 동길 형, 6개월간 후드 같이 쓴 선우, 후배 같지 않은 후배 상원, 이제 곧 미국에서 고생할 태교, 고등학생 같은데 교생 나가는 경민 그리고 이번 봄 학기부터 대학원생이 될 태훈,

희경, 학부생 때부터 고생한 보란, 석희, 지금은 실험실에 없지만 같이 생활했던 기포 형, 재훈 형, 성환, 여울, 수홍, 헌석, 희준, 소속은 달랐지만 많은 도움을 주었던 명수 형, 지현, 고려대에서 많은 도움을 주었던 경석 형, 동은 형, 지환 형, 종연 형, 재성, 현진, 현희, 윤희, 모두들이 있어 때론 고된 실험실 생활도 즐겁게 보낼 수 있었습니다. 정말 감사합니다.

그리고 마지막으로 저를 위해 헌신하신 저의 부모님과 누나와 매형에게 감사의 말을 전하고 싶습니다.

SPECTRA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1.05
1.08
0.95
3.16
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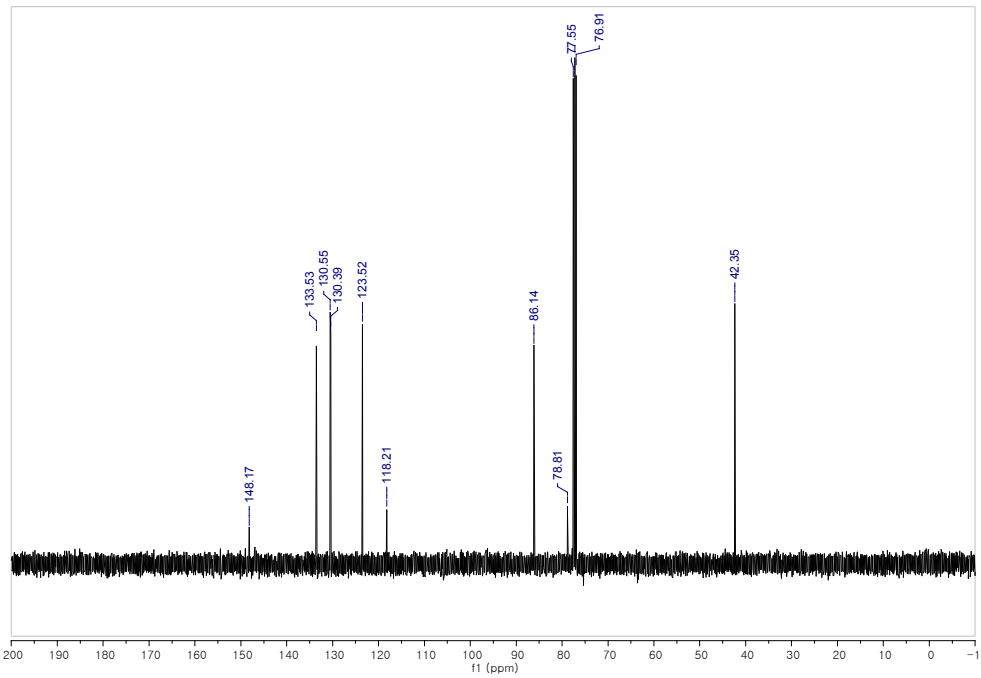
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76.91
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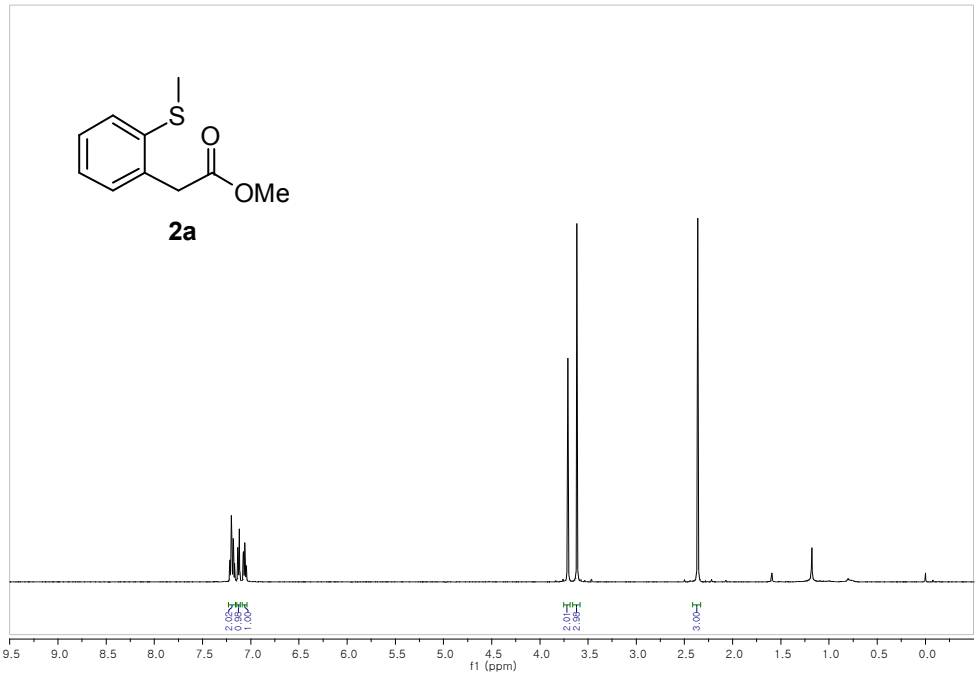
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OMe
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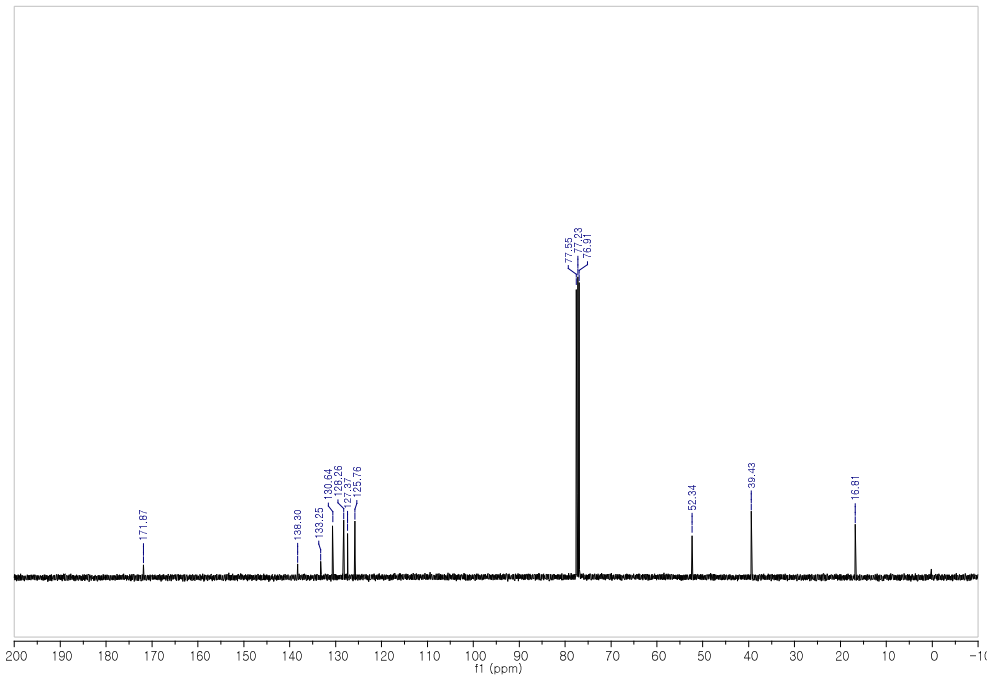
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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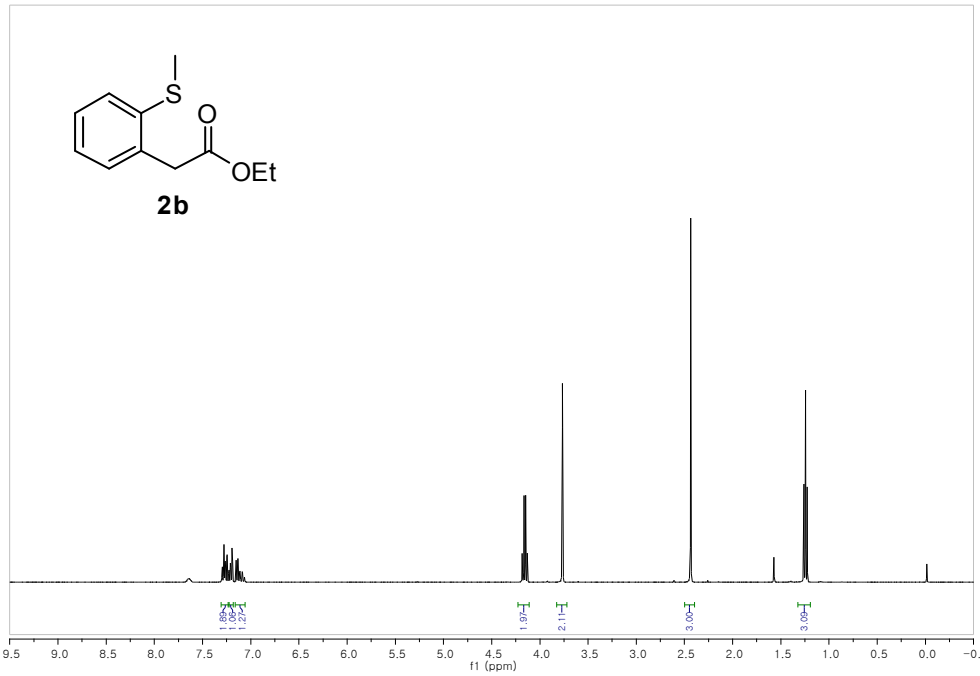
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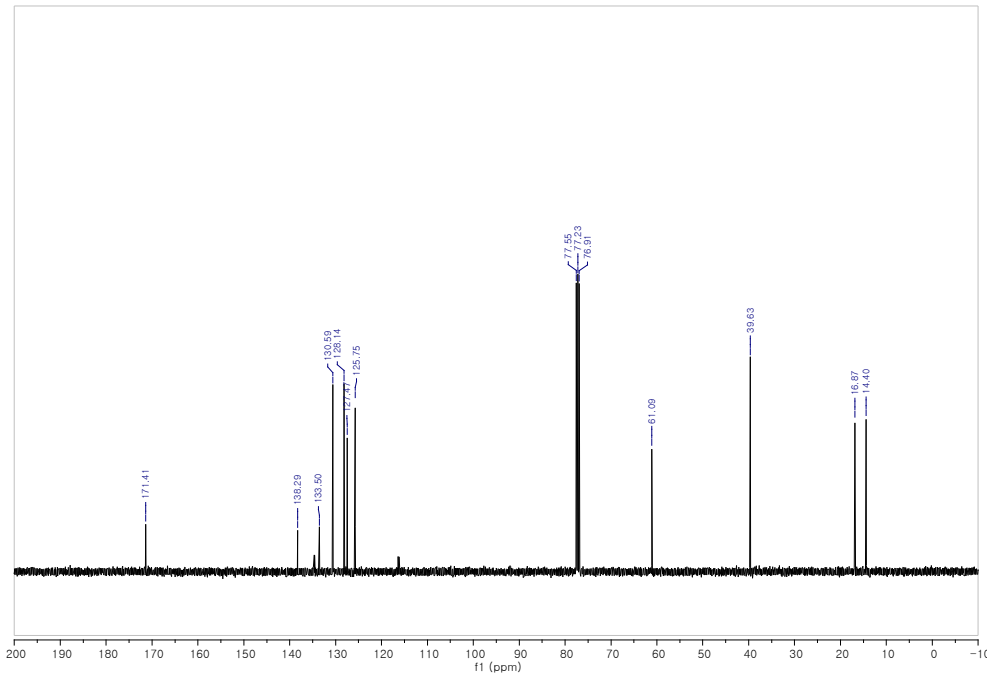
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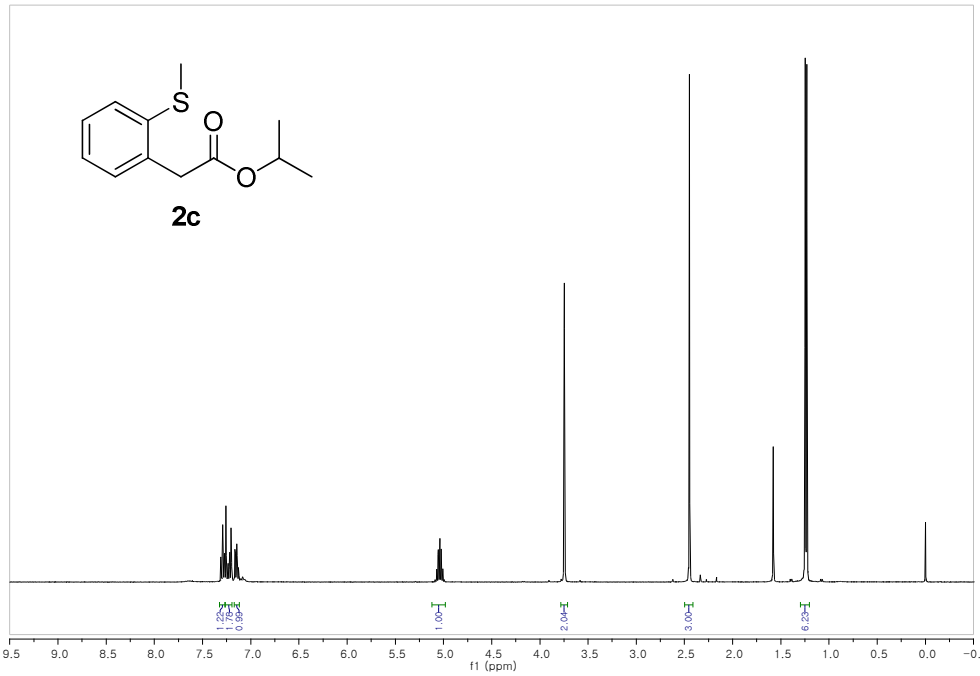
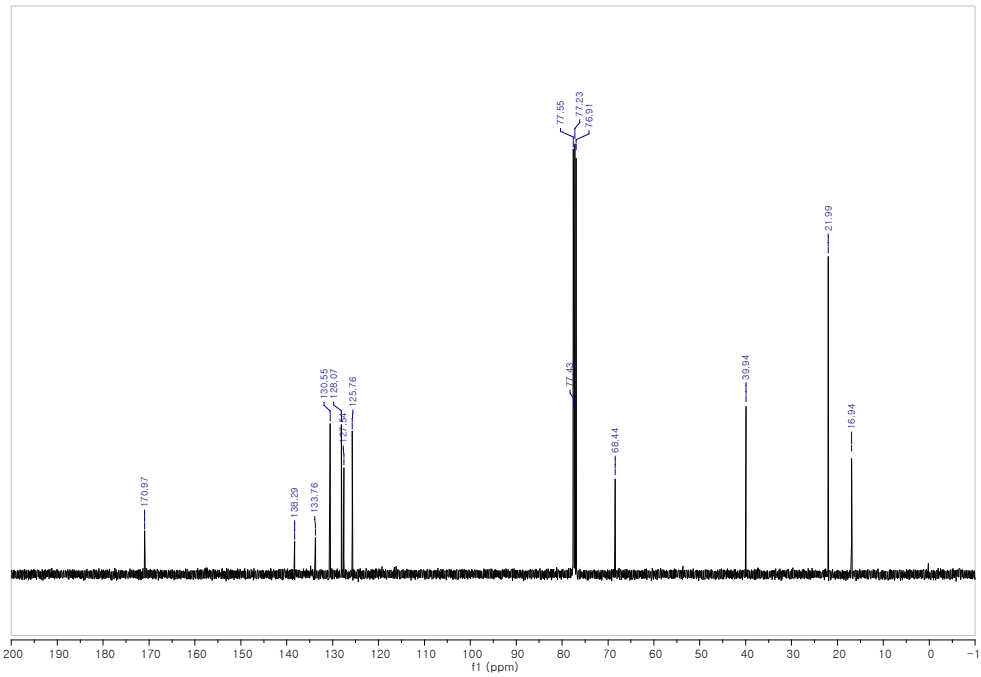
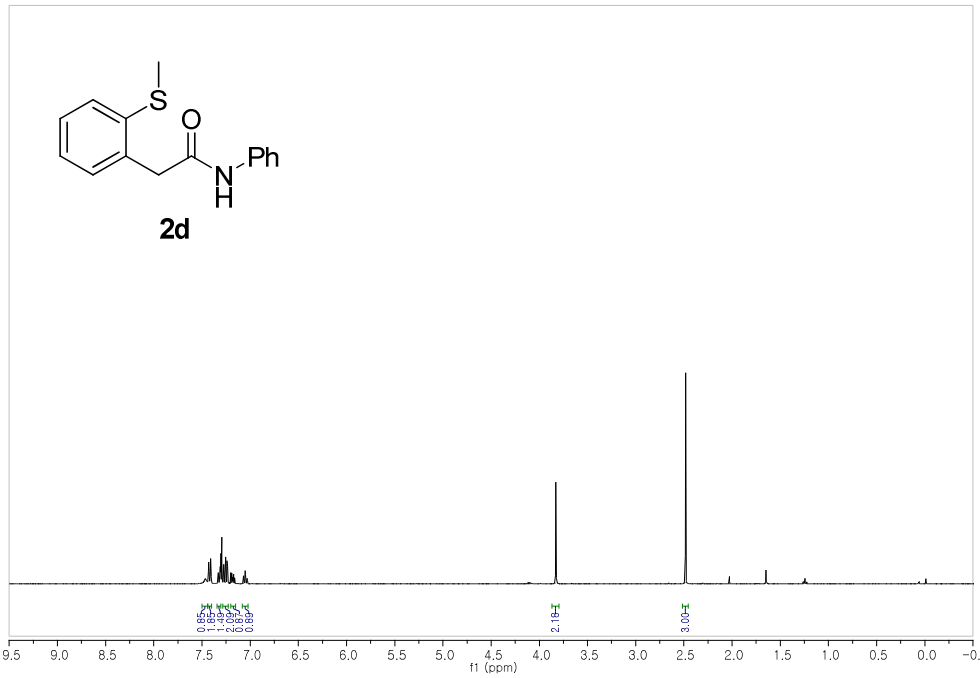
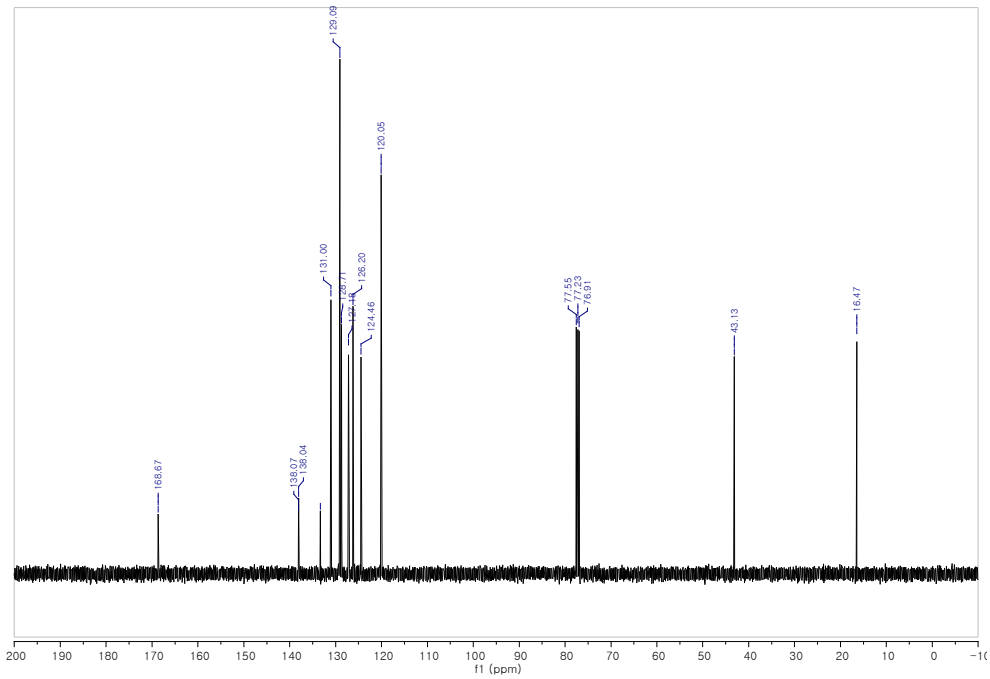
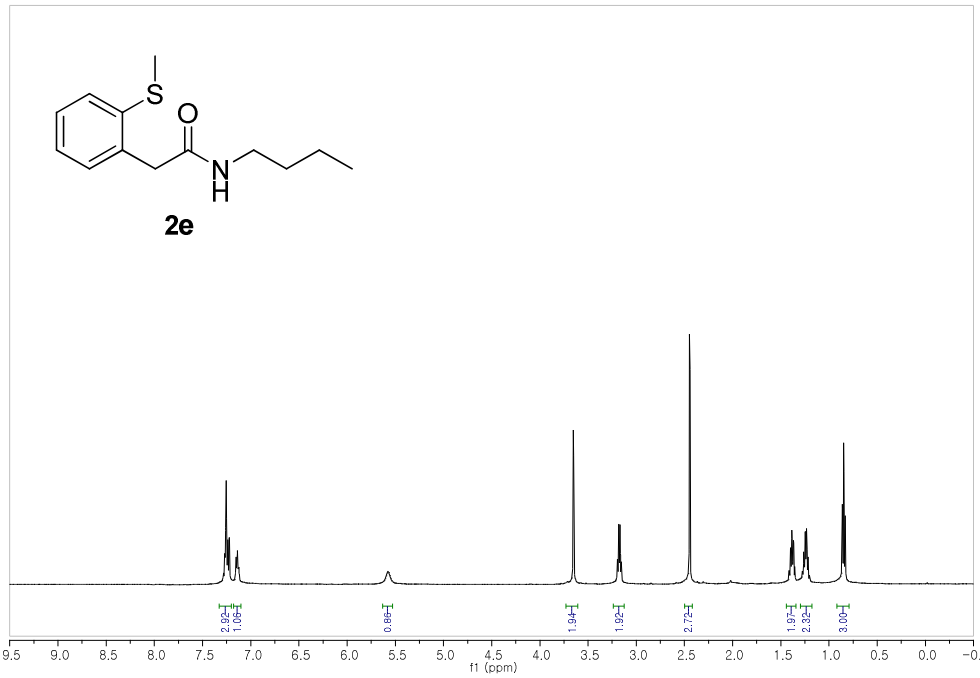
130.59
128.14
127.47
125.75
77.55
77.23
76.91
61.09
39.63
16.67
14.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

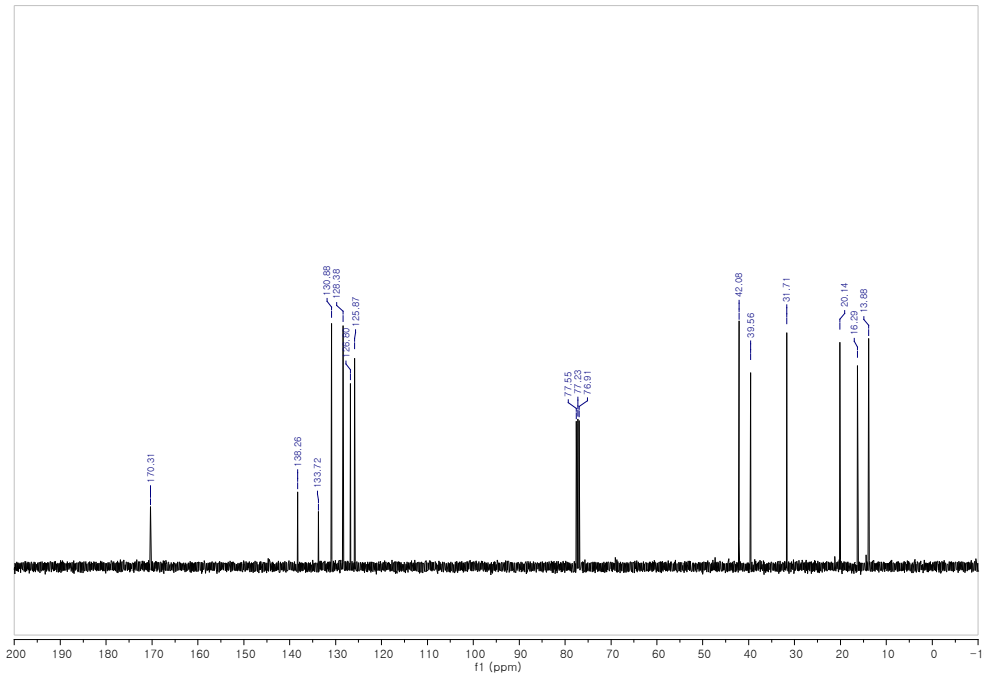

S
O
O
2c
1.20
1.22
1.00
0.99
1.00
2.04
3.00
6.22
f1 (ppm)

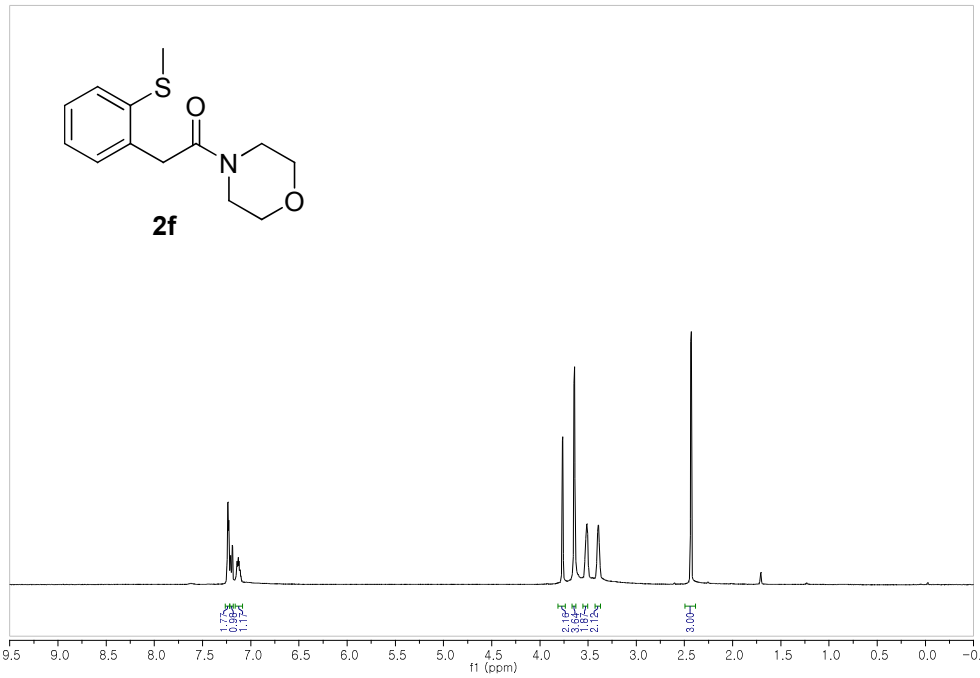

77.55
77.23
76.91
77.43
170.97
138.29
133.76
130.55
128.07
125.76
68.44
39.94
21.99
16.94
f1 (ppm)

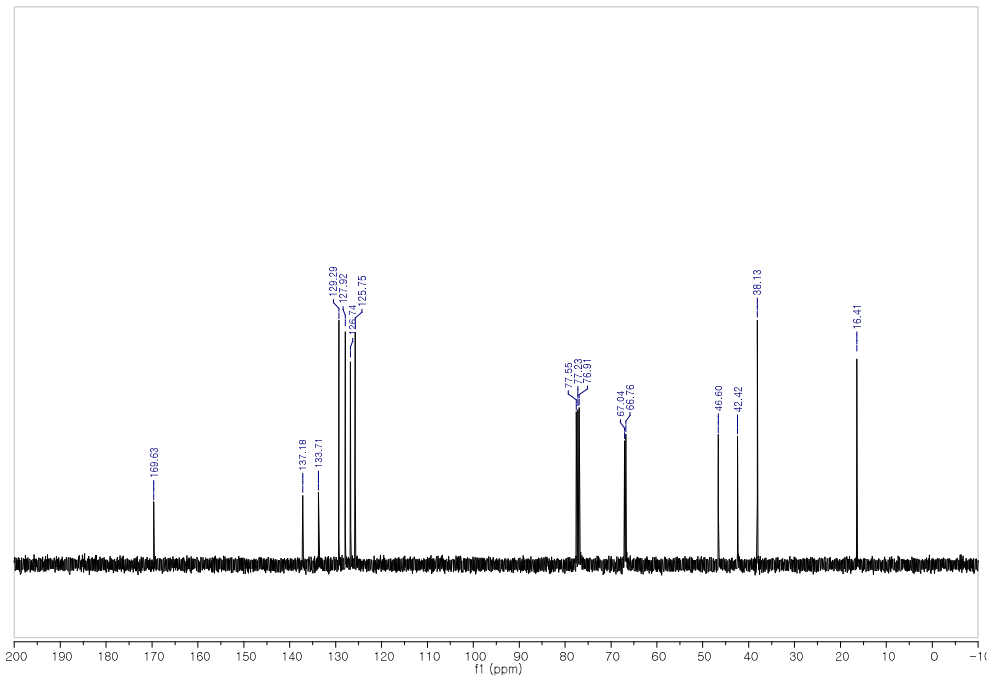

S
O
N
H
Ph
2d
2.16
3.00
f1 (ppm)

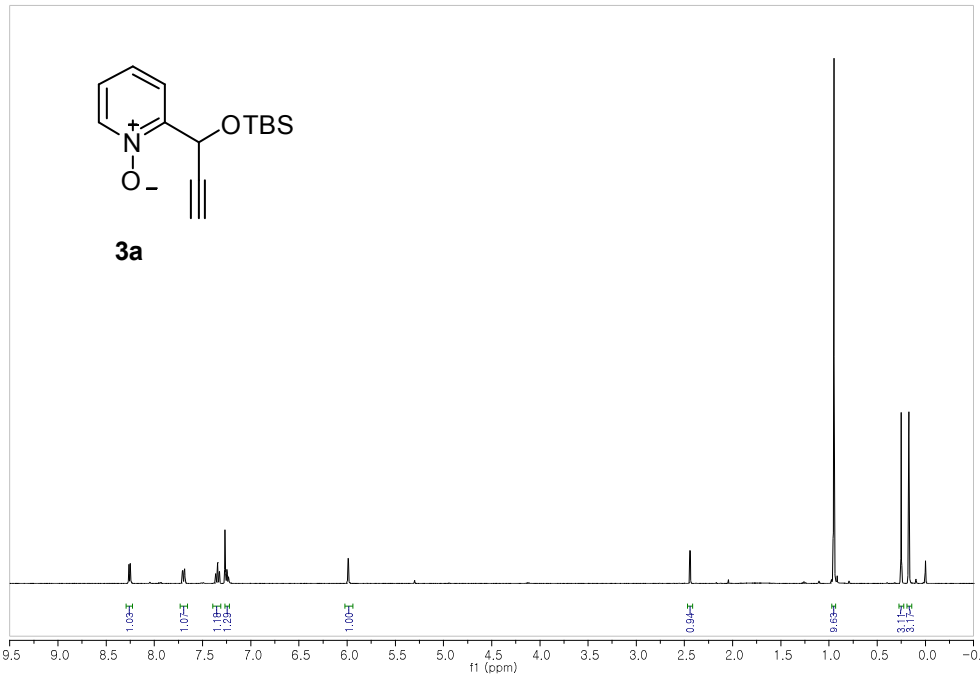

168.67
138.07
136.04
131.00
129.09
126.71
126.20
124.46
120.05
77.55
77.23
76.91
43.13
16.47
f1 (ppm)

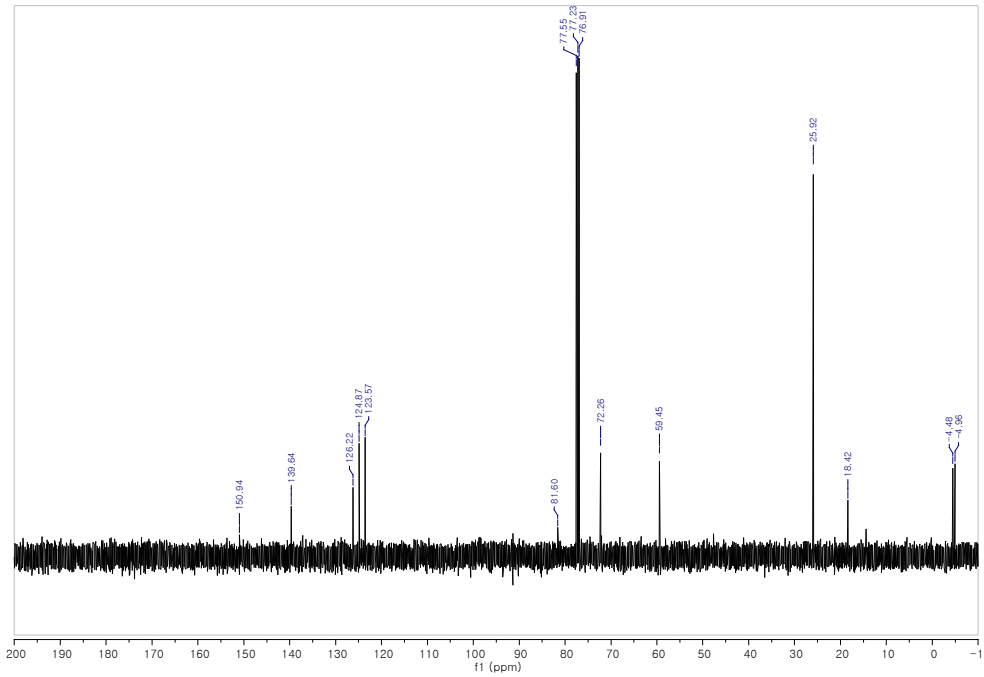

S
O
N
H
2e
2.92
1.06
0.86
1.94
1.92
2.74
1.97
2.32
3.00
f1 (ppm)

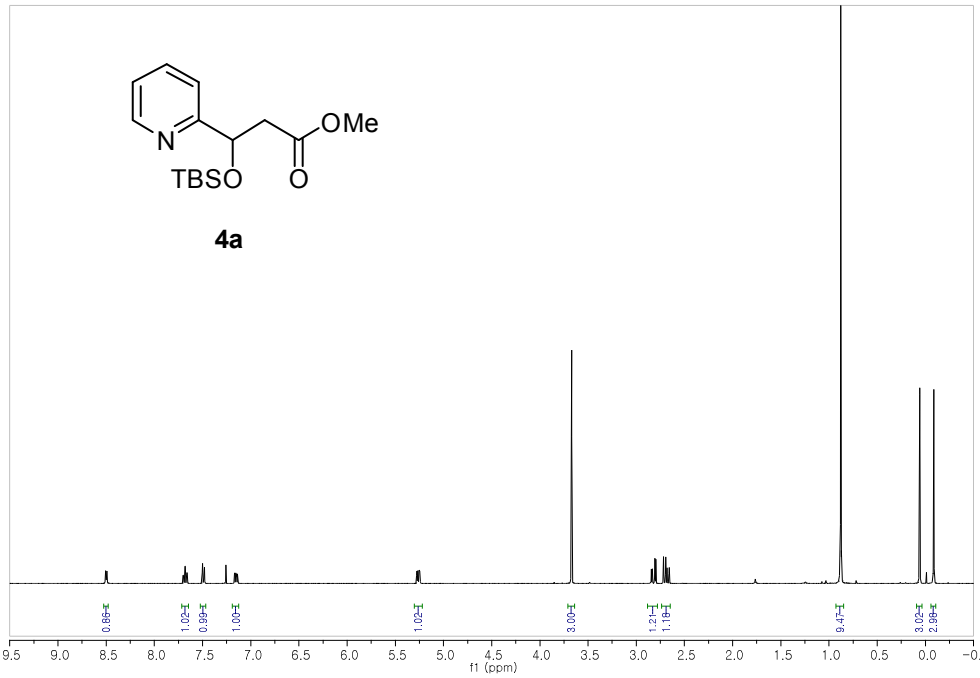

170.31
138.26
133.72
130.88
128.38
126.80
125.87
77.55
77.23
76.91
42.08
39.56
31.71
20.14
18.29
13.88
f1 (ppm)


S
O
N
O
2f
1.77
0.99
1.11
2.16
3.64
1.85
2.15
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

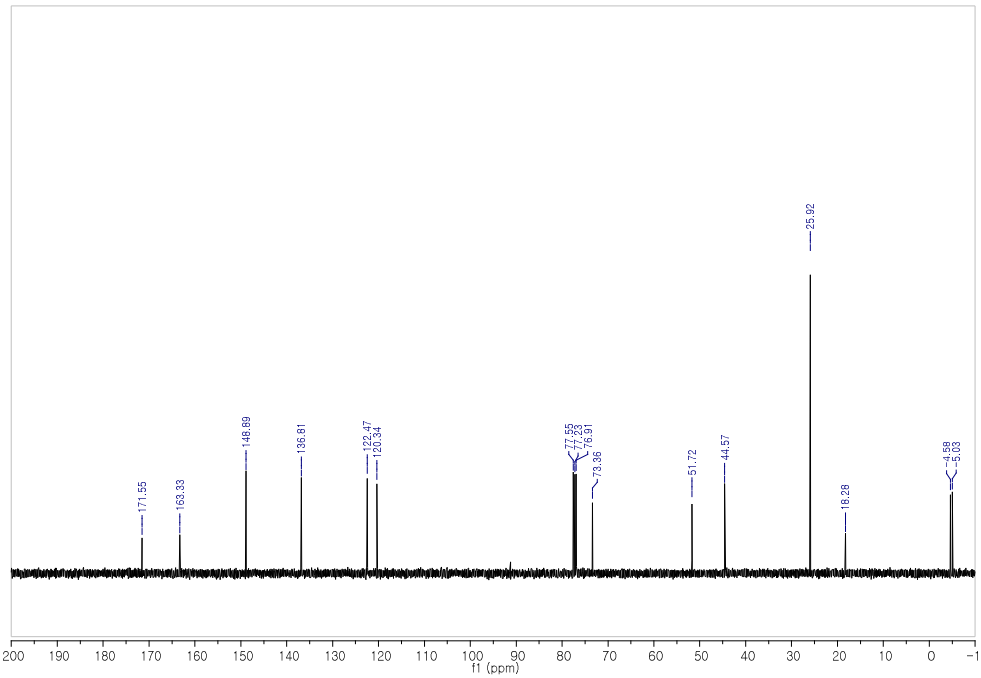

169.63
137.18
133.71
129.29
127.92
126.74
125.75
77.55
77.23
76.91
67.04
66.76
46.60
42.42
38.13
16.41
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

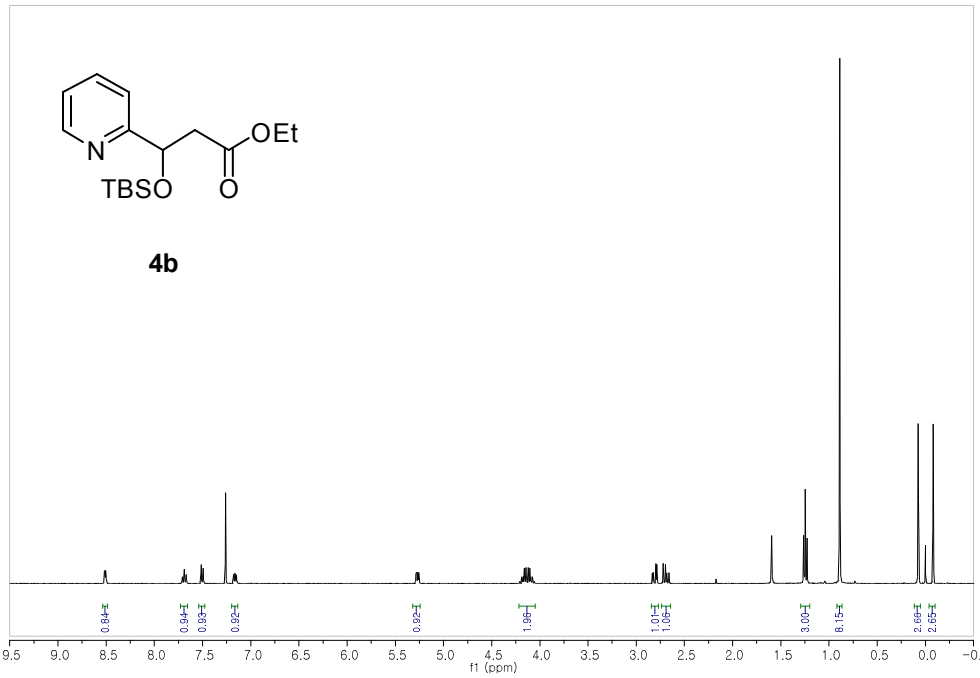

OTBS
N
O
3a
1.03
1.07
1.18
1.25
1.00
0.94
9.63
3.11
3.17
f1 (ppm)

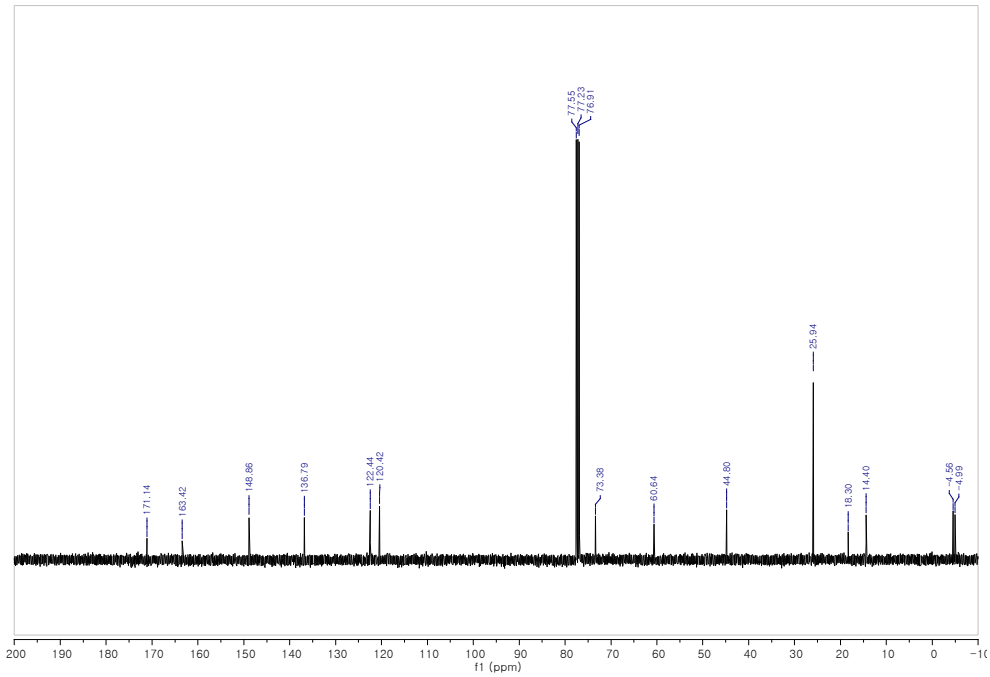

77.55
77.23
76.91
25.92
72.26
59.45
150.94
139.64
126.22
124.87
123.57
81.60
18.42
-4.48
-4.96
f1 (ppm)

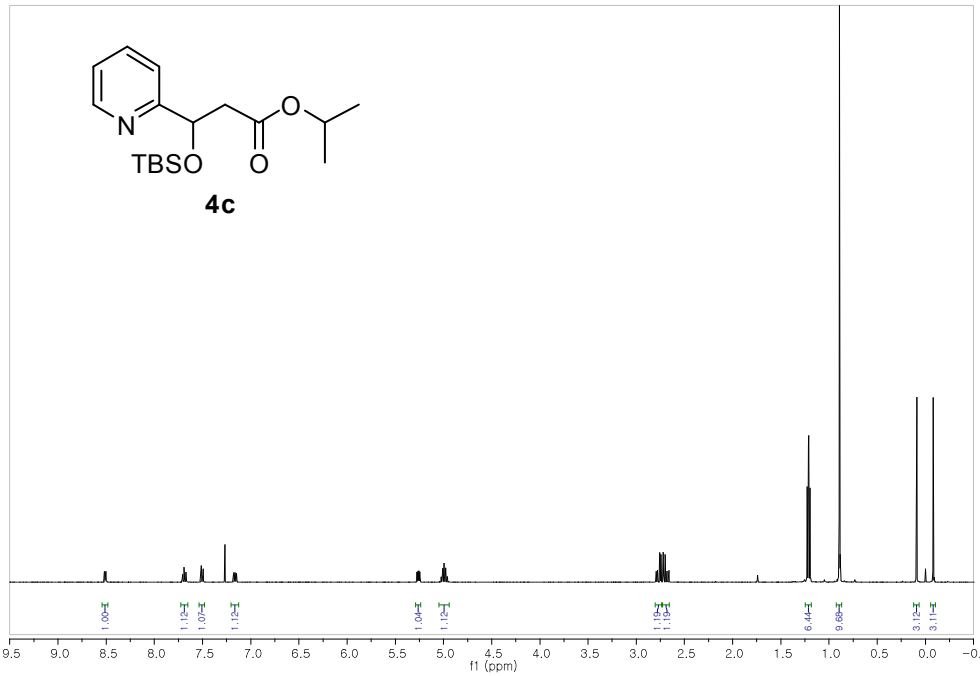

N
OMe
TBSO
O
0.86
1.02
0.99
1.00
1.02
3.00
1.21
1.16
9.47
3.02
2.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.
f1 (ppm)

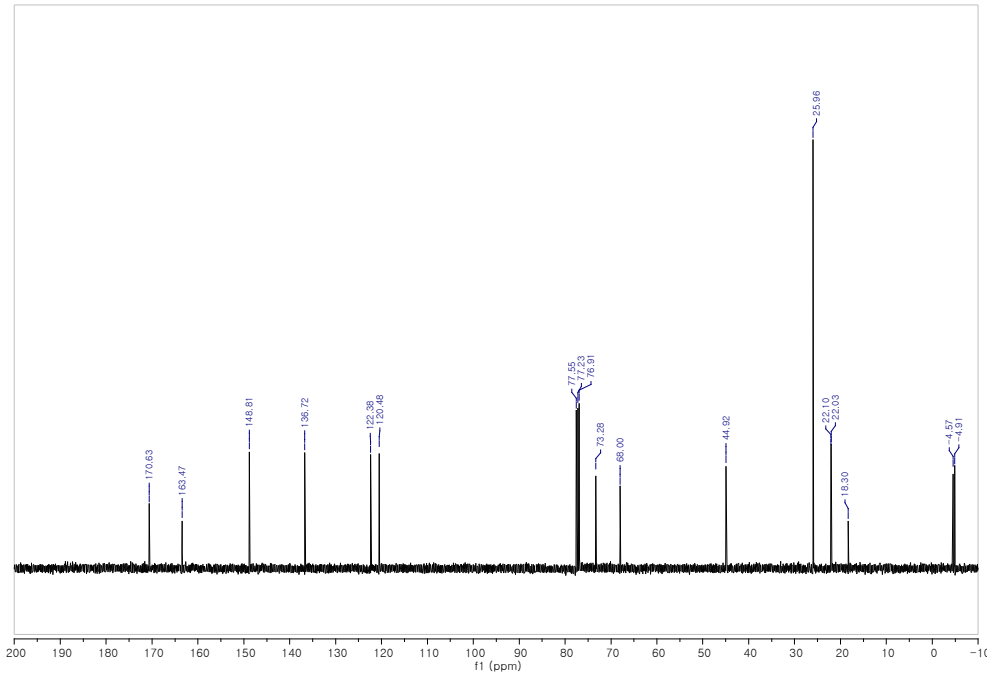
4a


171.55
163.33
148.89
136.81
122.47
120.34
77.55
77.23
76.91
73.36
51.72
44.57
25.92
18.28
-4.58
-5.03
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1
f1 (ppm)


OEt
N
TBSO
O
4b
0.84
0.94
0.93
0.92
0.92
1.96
1.01
1.06
3.00
8.15
2.66
2.65
f1 (ppm)


77.55
77.23
76.91
171.14
163.42
148.86
136.79
122.44
120.42
73.38
60.64
44.80
25.94
18.30
14.40
-4.56
-4.99
f1 (ppm)


N
TBSO
O
O
4c
1.00
1.12
1.07
1.12
1.04
1.12
1.15
1.15
6.44
9.69
3.13
3.11
f1 (ppm)


170.63
163.47
148.81
136.72
122.38
120.48
77.55
77.23
76.91
73.28
66.00
44.92
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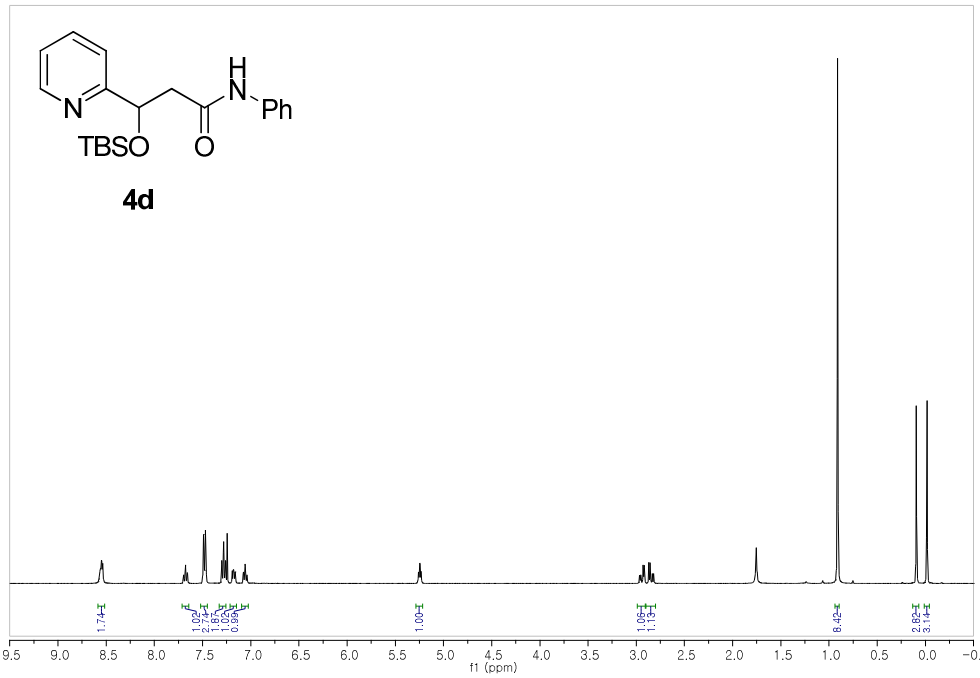
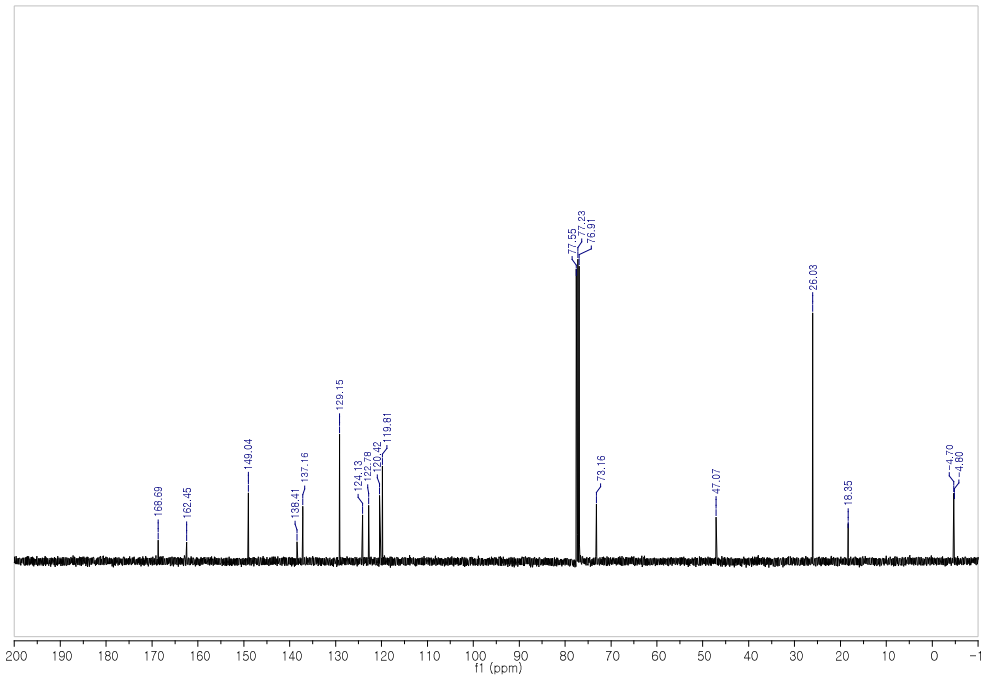
22.03
18.30
-4.57
-4.91
f1 (ppm)


TBSO
O
H
N
Ph
4d
f1 (ppm)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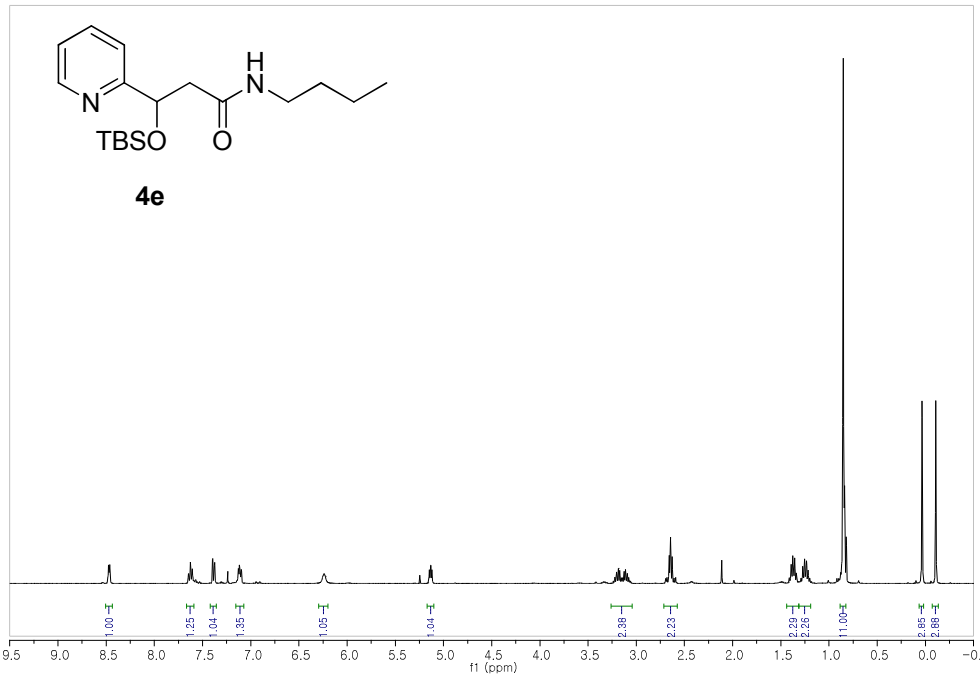
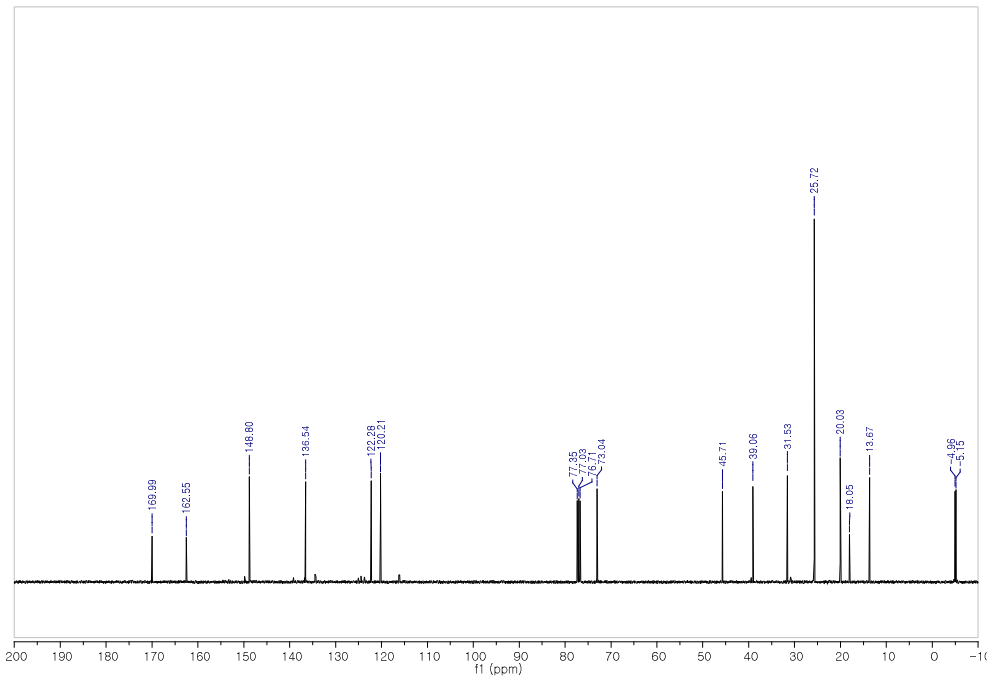
162.45
149.04
138.41
137.16
129.15
124.13
122.78
120.40
119.81
77.55
77.23
76.91
73.16
47.07
26.03
18.35
4.70
4.80
f1 (ppm)


H
N
N
TBSO
O
4e
1.00
1.25
1.04
1.35
1.05
1.04
2.38
2.23
2.28
2.28
11.00
2.85
2.88
f1 (ppm)


169.99
162.55
148.80
136.54
122.28
120.21
77.05
77.00
76.71
73.04
45.71
39.06
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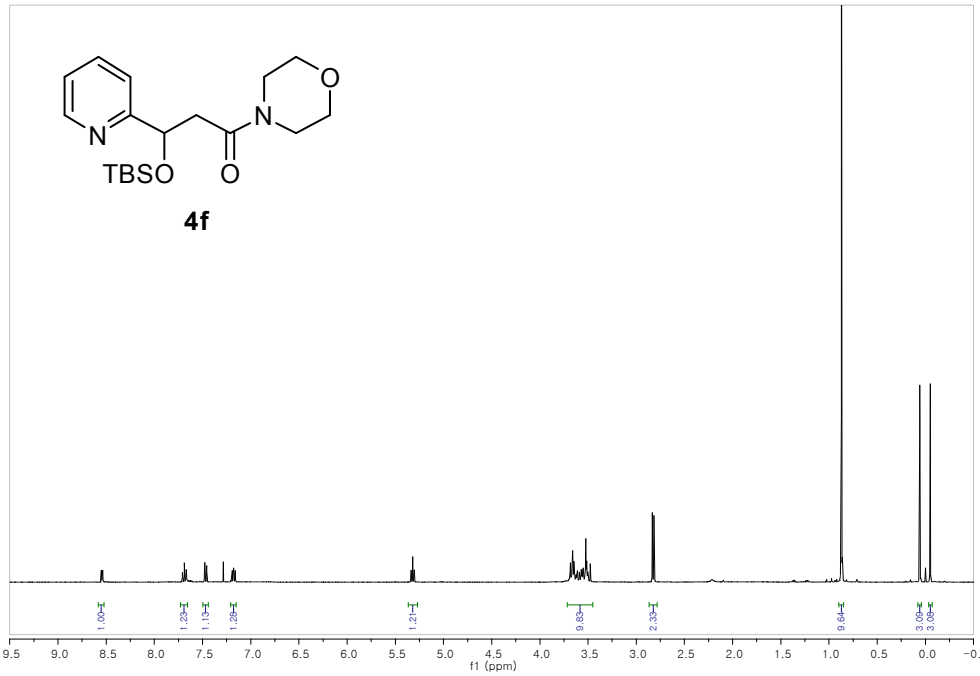
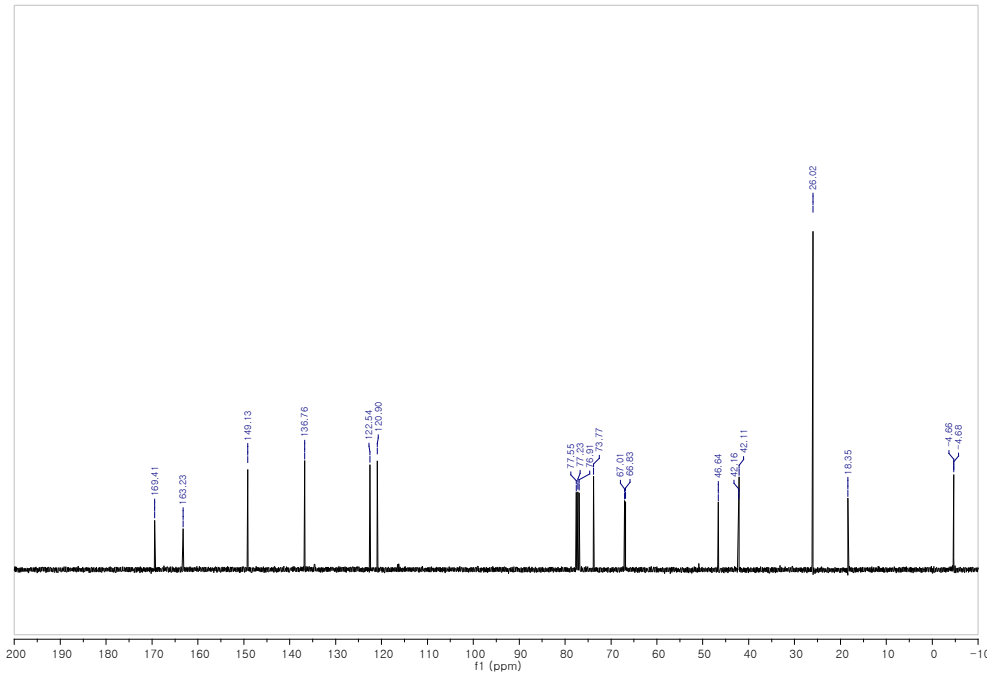
25.72
20.03
18.05
13.67
f1 (ppm)


TBSO
O
N
O
N
1.00
1.29
1.19
1.28
1.21
9.83
2.33
9.64
3.09
3.08
f1 (ppm)

4f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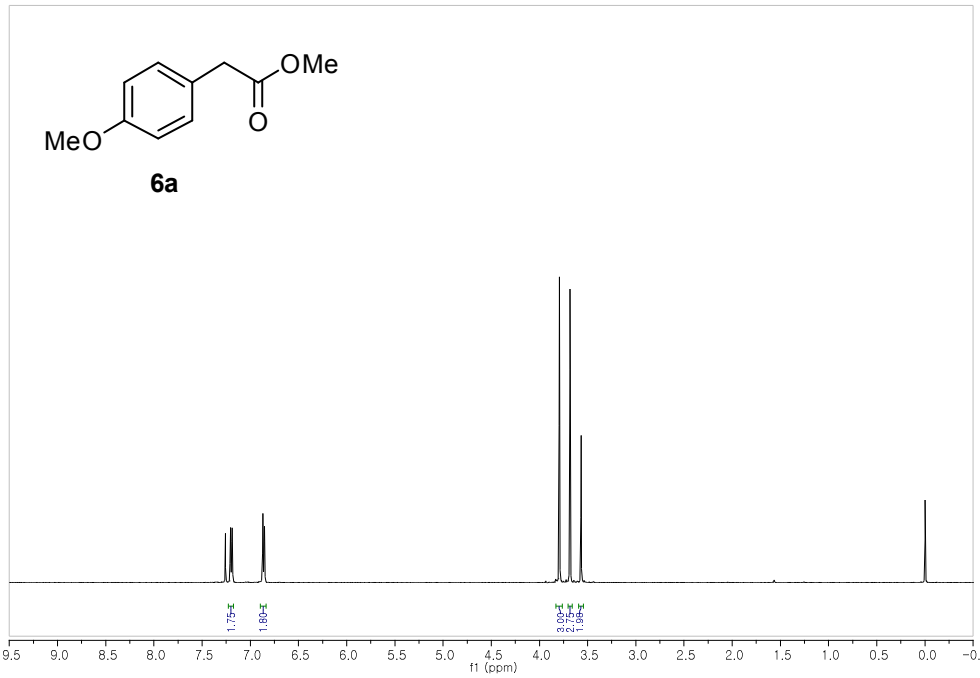
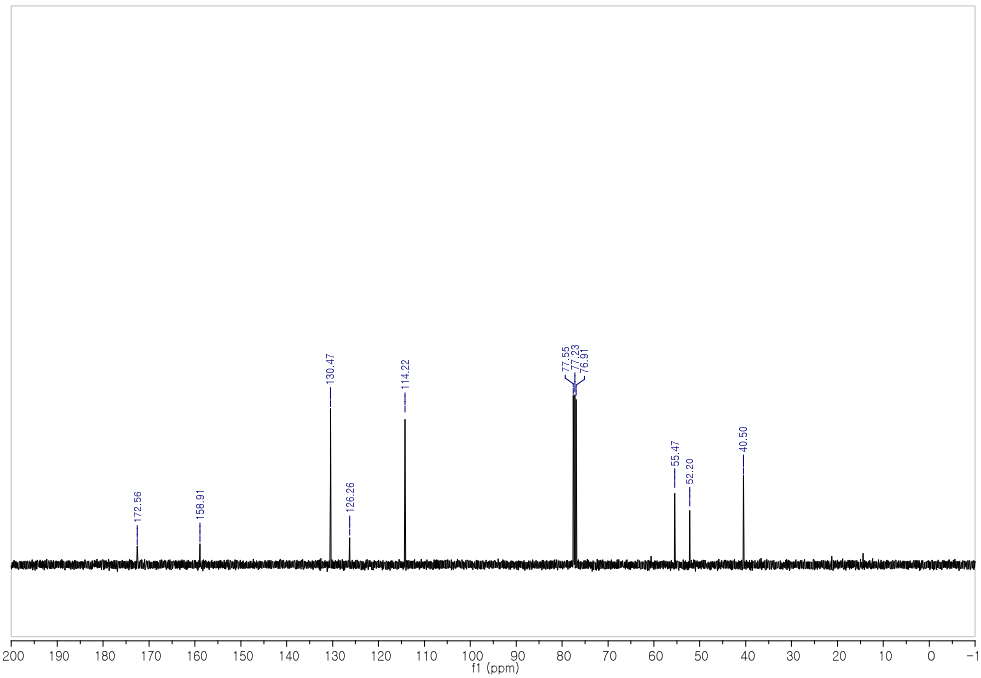
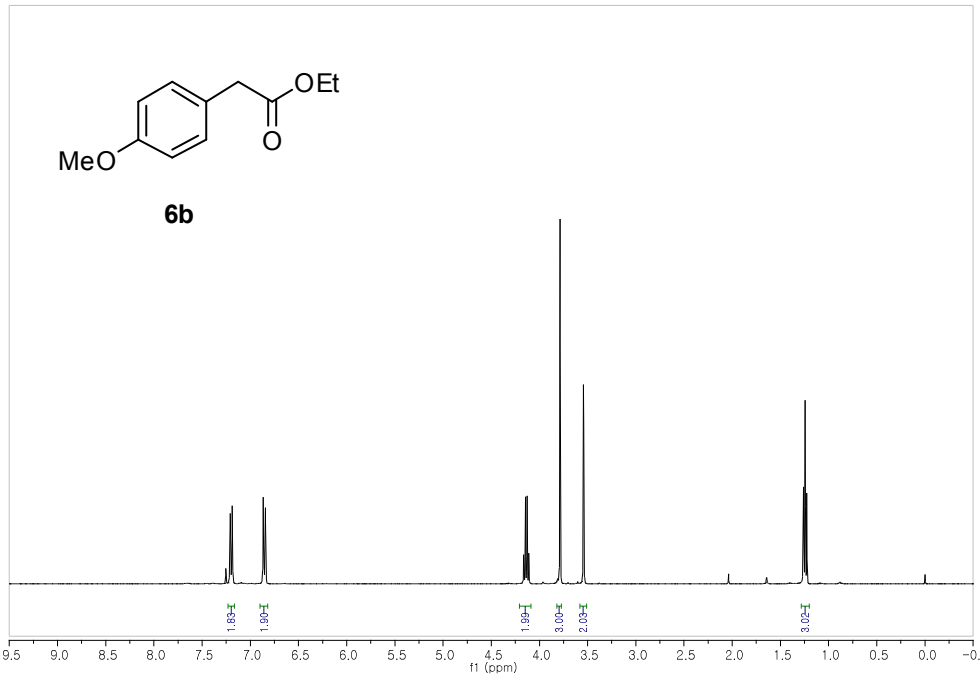
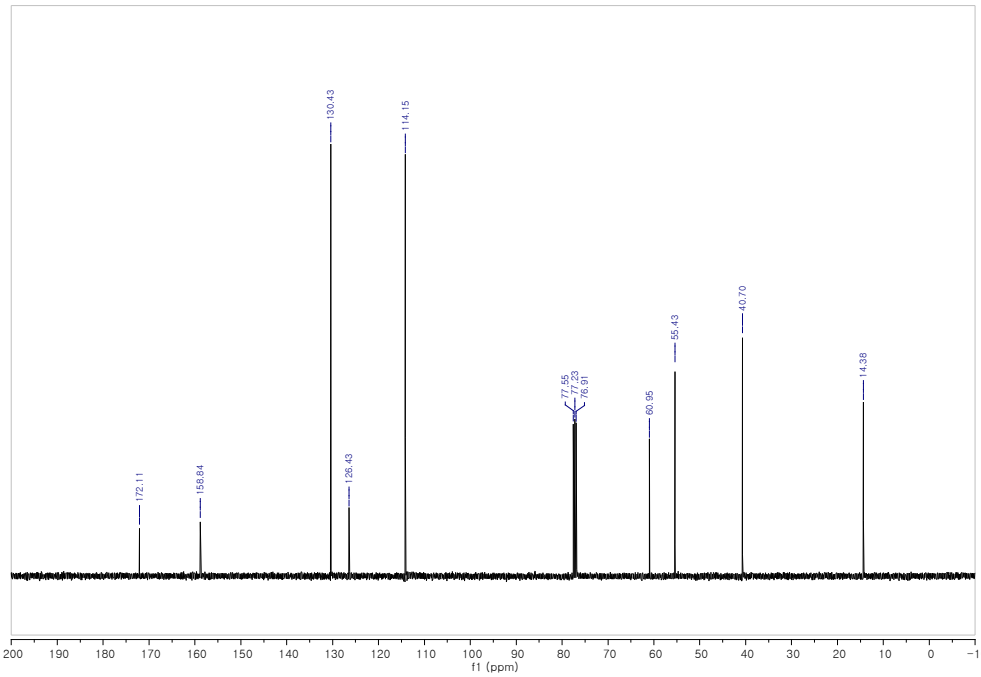
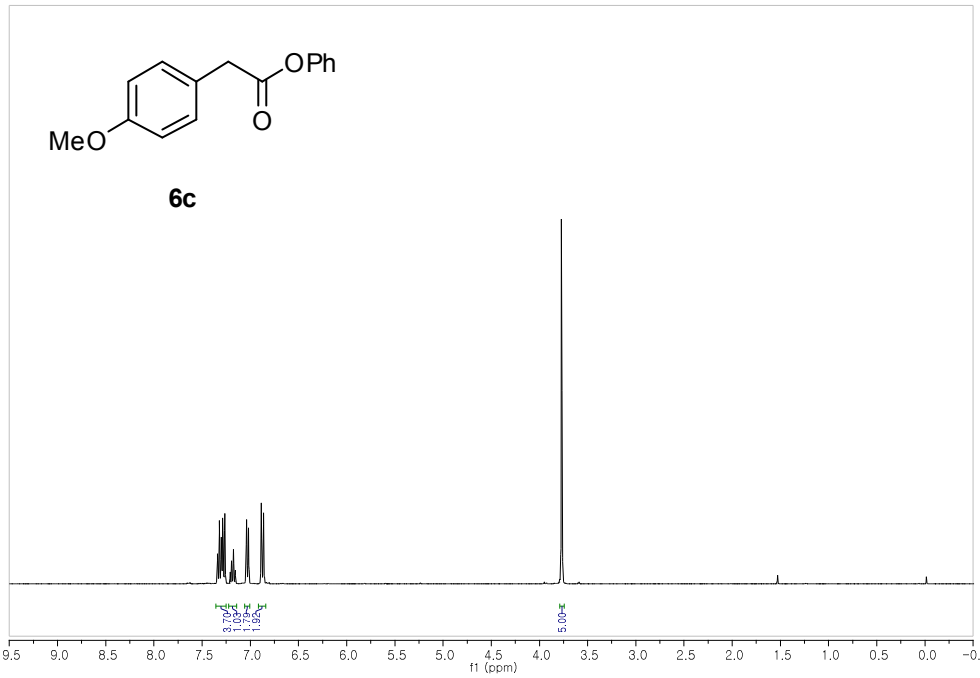
163.23
149.13
136.76
122.54
120.90
77.55
77.23
76.91
73.77
67.01
66.83
46.64
42.16
42.11
26.02
18.35
-4.66
-4.69
f1 (ppm)

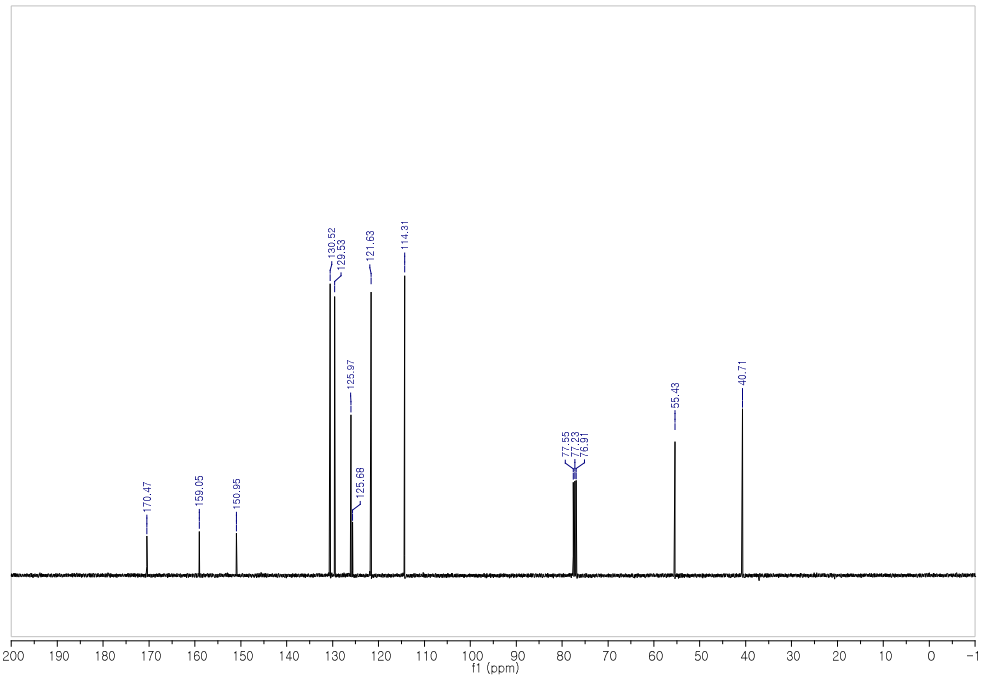

OMe
O
MeO
6a
1.75
1.80
3.00
2.75
1.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

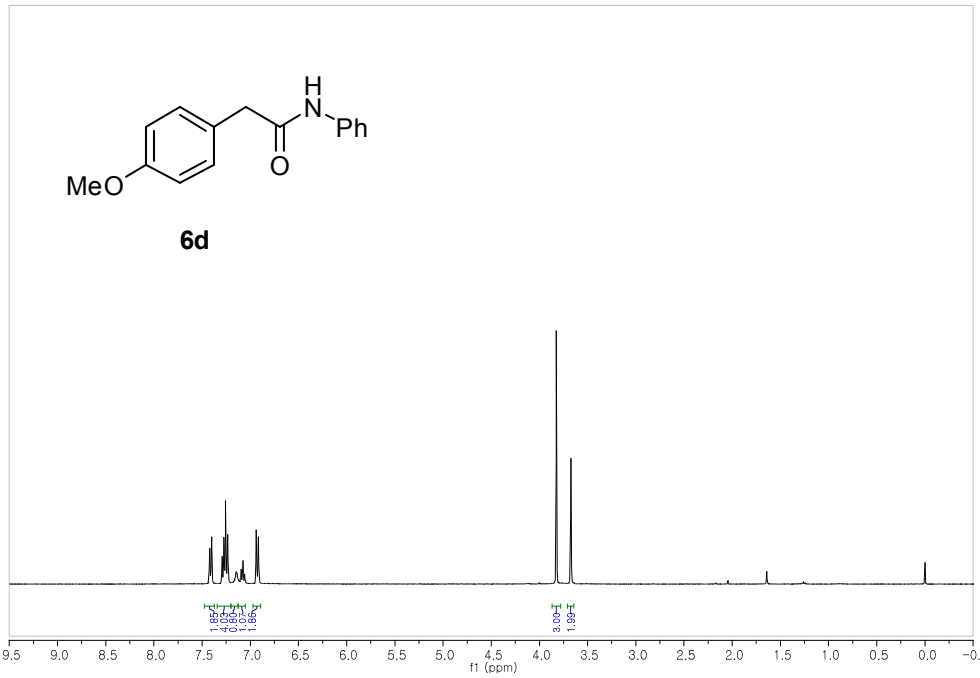

172.56
158.91
130.47
126.26
114.22
77.55
77.23
76.91
55.47
52.20
40.50
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OEt
O
MeO
6b
1.89
1.90
1.99
3.00
2.03
3.02
f1 (ppm)

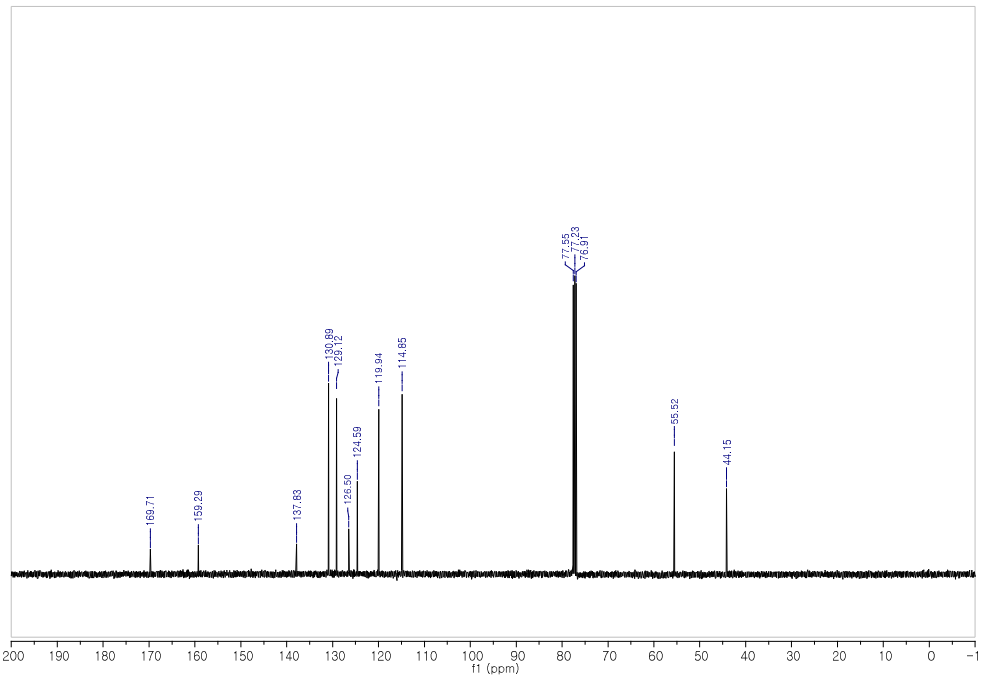

130.43
114.15
172.11
158.84
126.43
77.55
77.23
76.91
60.95
55.43
40.70
14.38
f1 (ppm)

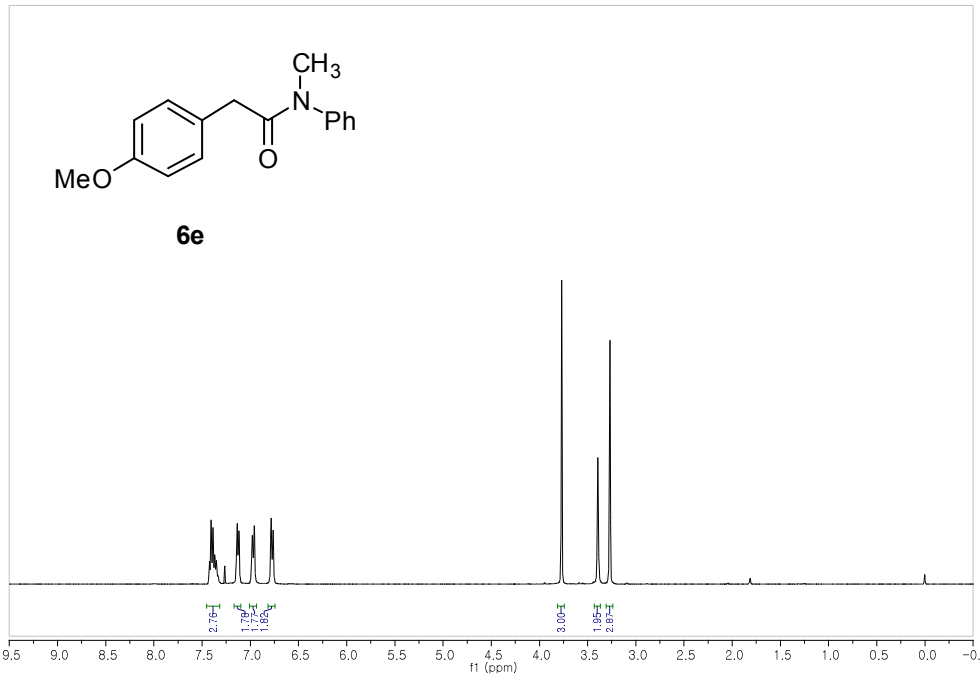

OPh
O
MeO
6c
3.70
1.03
1.00
1.98
5.00
f1 (ppm)


170.47
159.05
150.95
130.52
129.53
125.97
125.68
121.63
114.31
77.55
77.23
76.91
55.43
40.71
f1 (ppm)

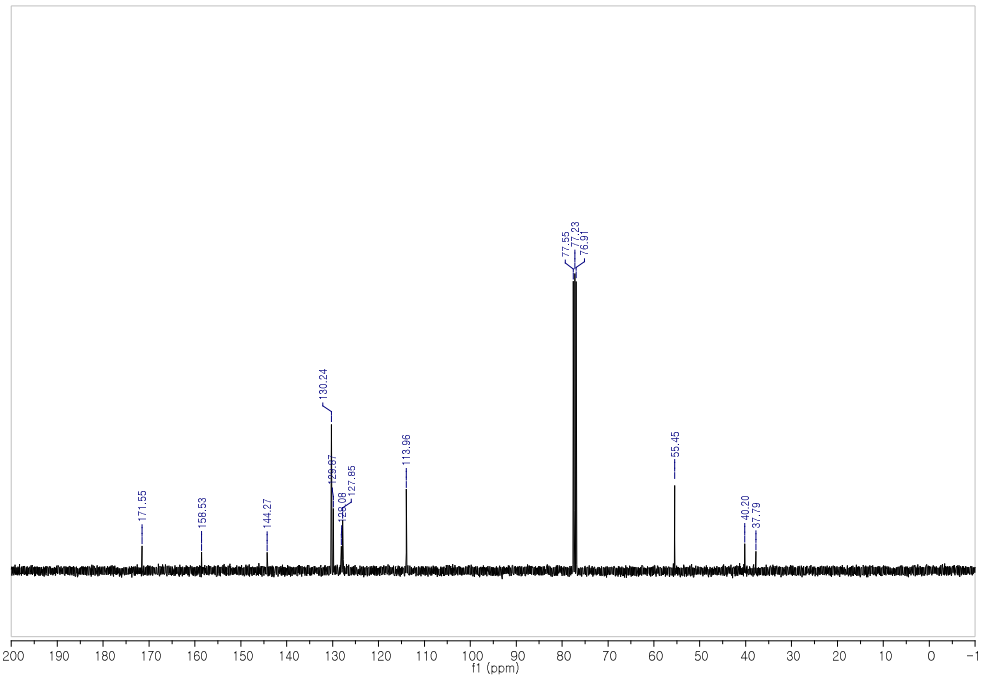

H
N
Ph
O
MeO
1.85
4.03
0.85
1.86
3.00
1.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

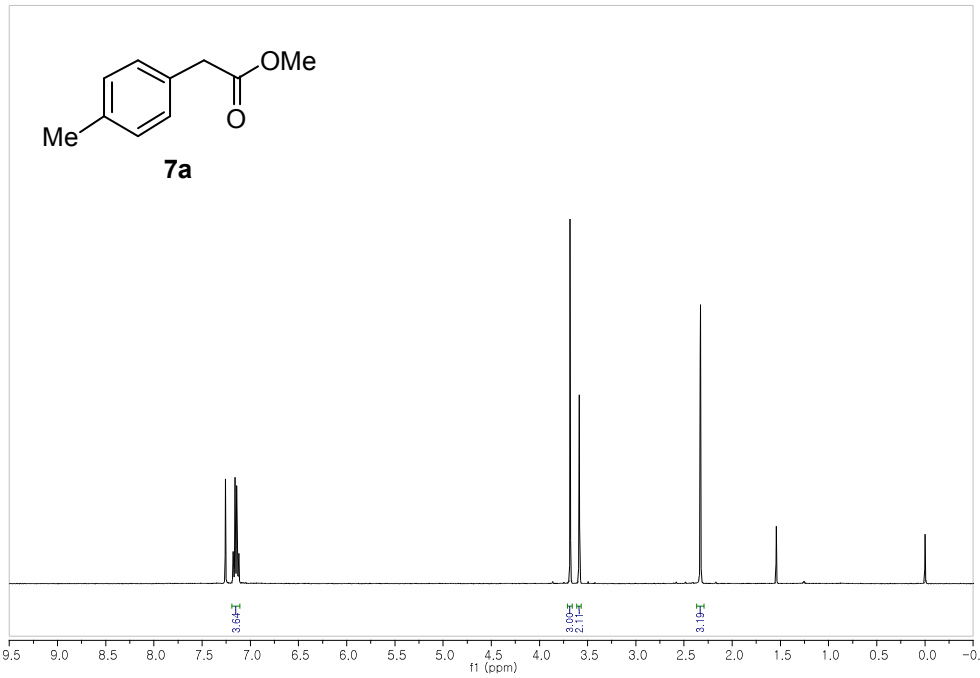
6d

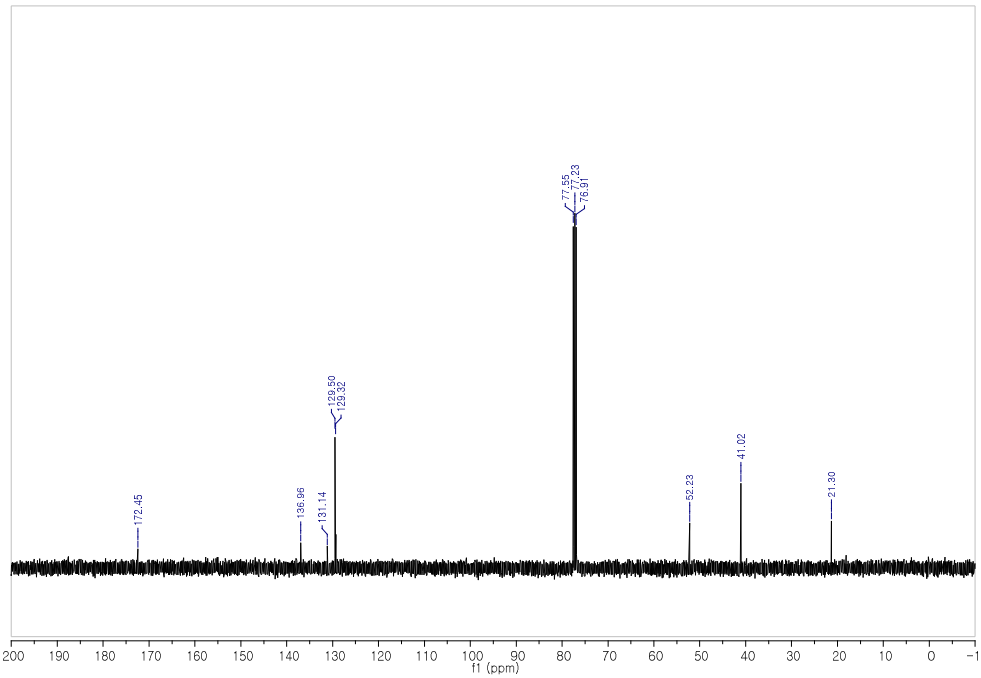

169.71
159.29
137.83
130.89
129.12
126.50
124.59
119.94
114.85
77.55
77.23
76.91
55.52
44.15
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

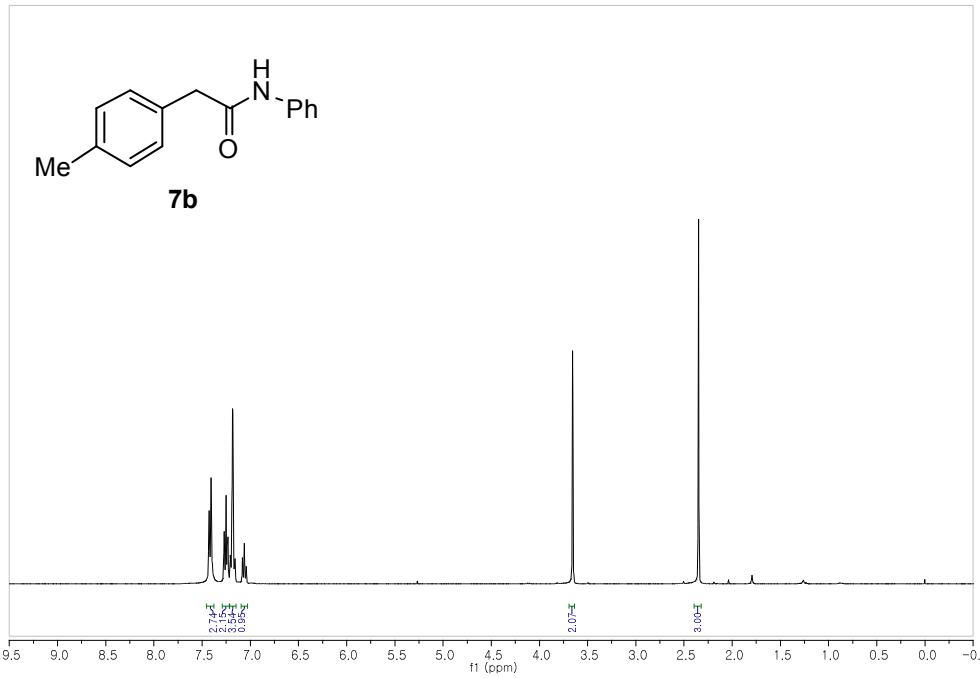

CH3
N
Ph
O
MeO
2.76
1.79
1.72
1.85
3.00
1.95
2.81
f1 (ppm)

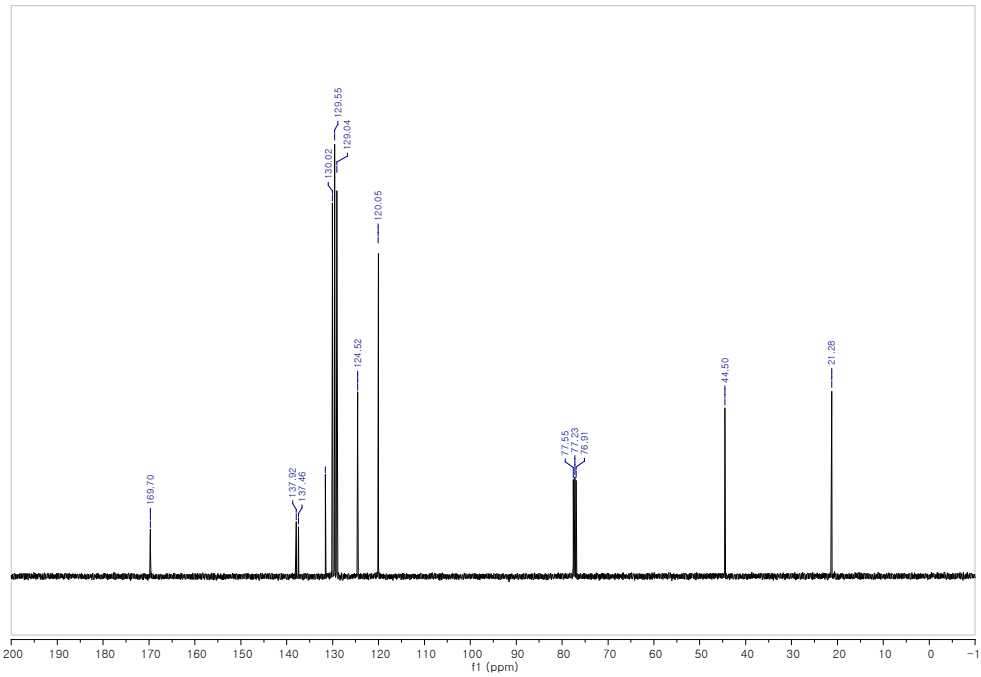
6e

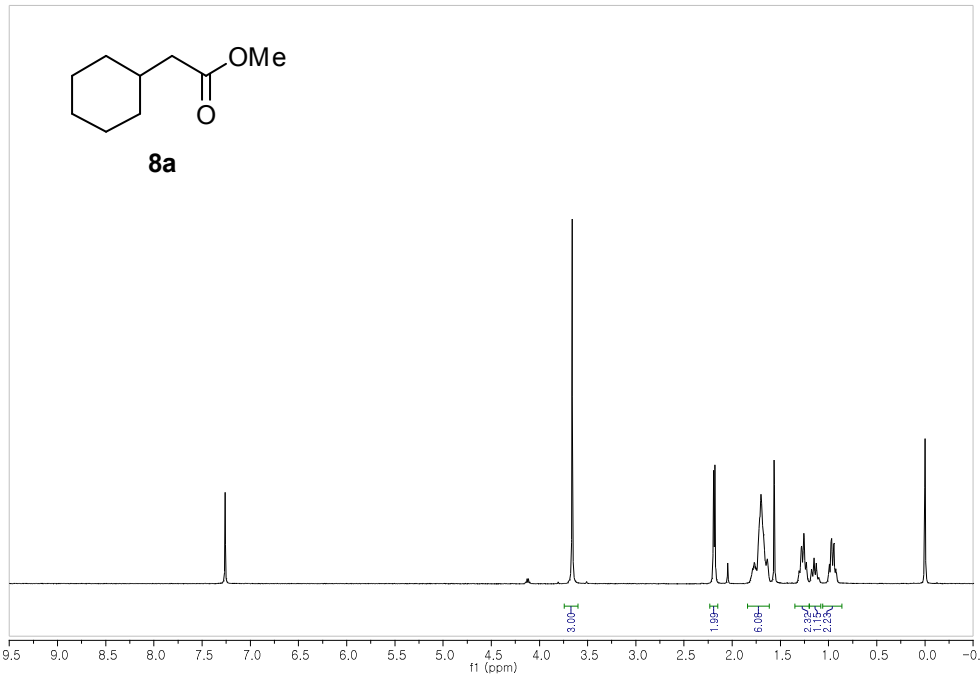

171.55
158.53
144.27
130.24
129.67
128.08
127.85
113.96
77.55
77.23
76.91
55.45
40.20
37.79
f1 (ppm)

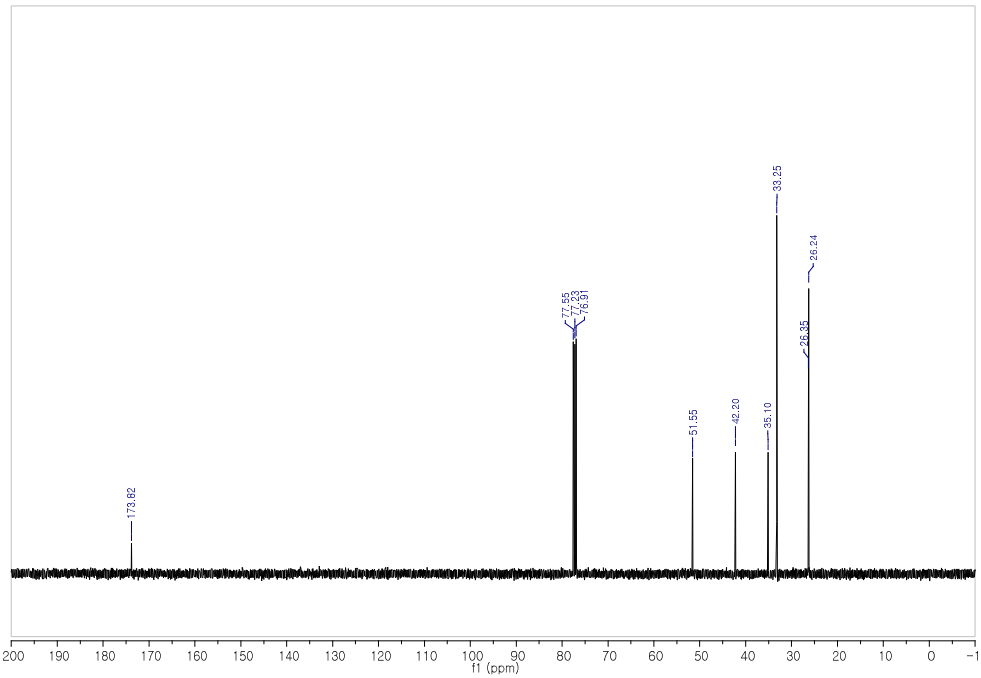

OMe
O
Me
7a
3.64
2.01
2.11
3.19
f1 (ppm)

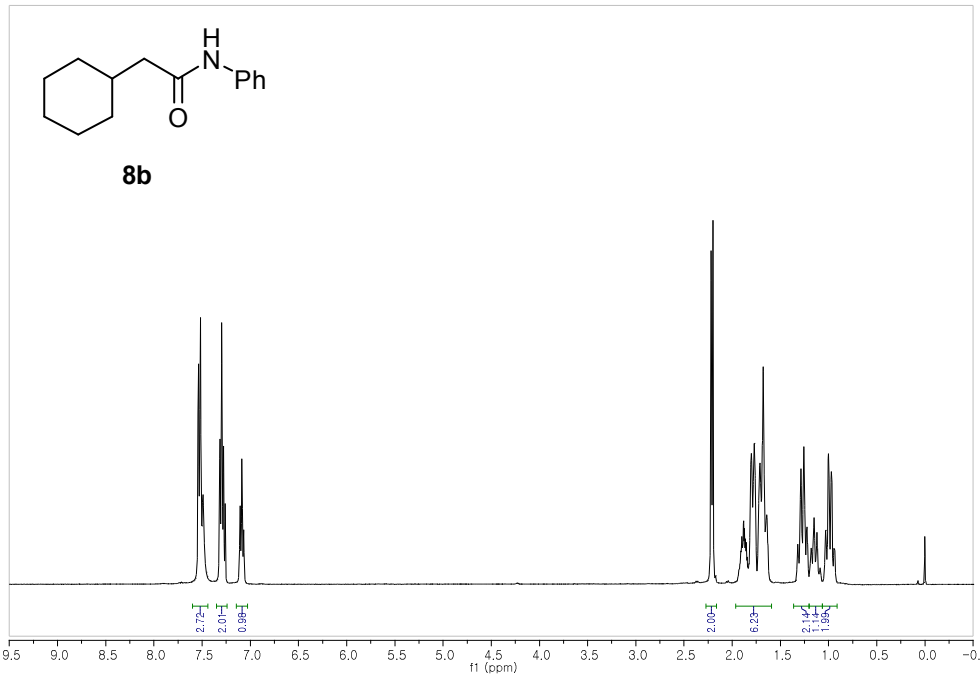

77.55
77.23
76.91
129.50
129.32
172.45
136.96
131.14
52.23
41.02
21.30
f1 (ppm)

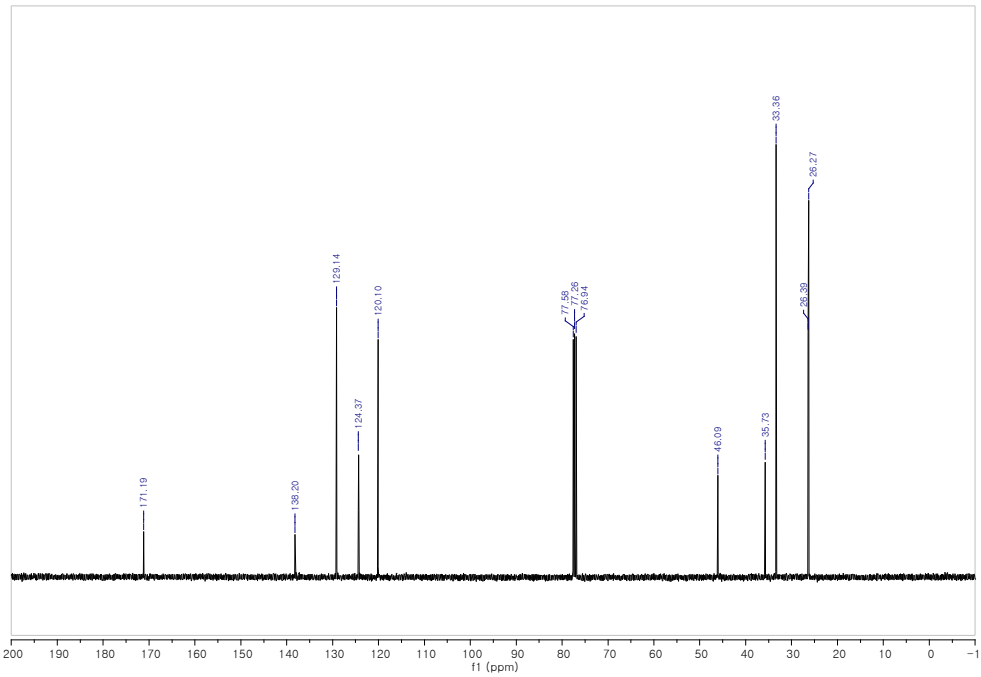

H
N
Ph
O
Me
7b
2.74
2.15
2.14
0.94
2.07
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

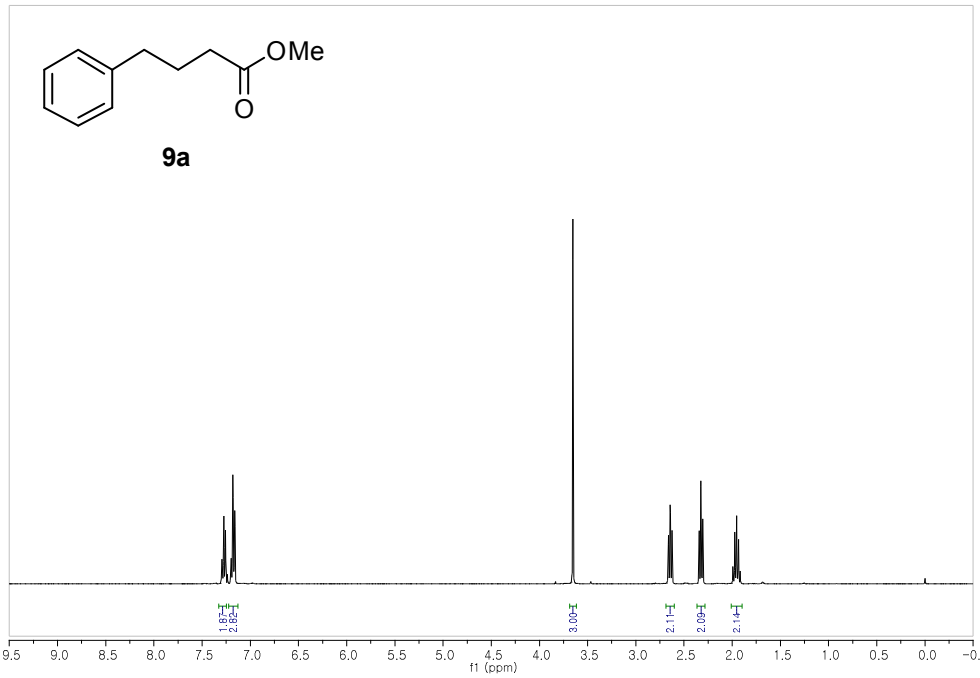

169.70
137.92
137.46
130.02
129.55
129.04
124.52
120.05
77.55
77.23
76.91
44.50
21.28
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

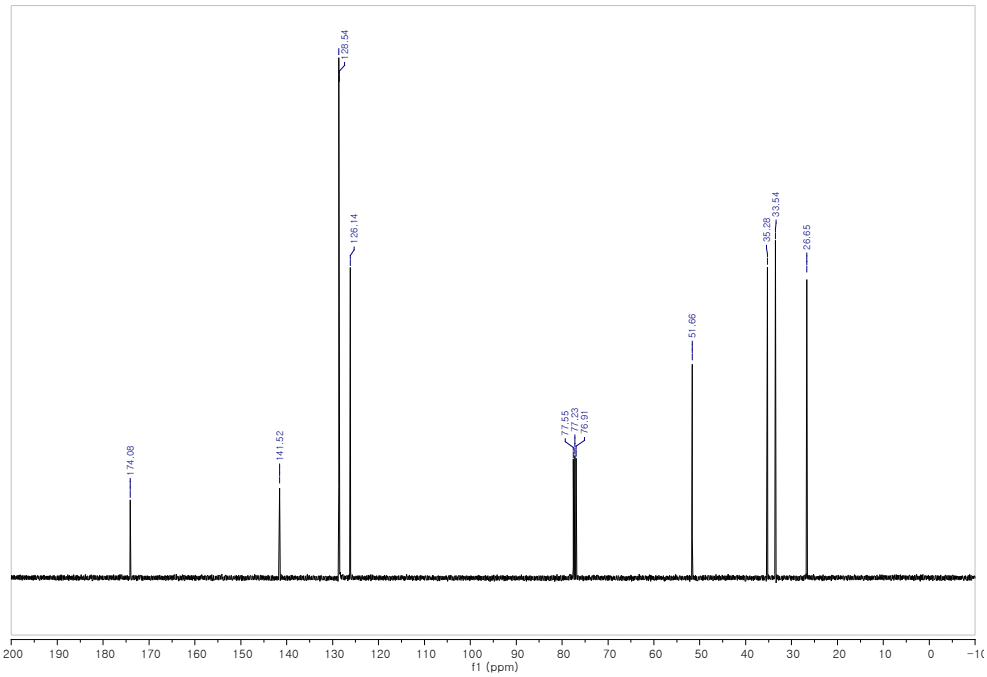

OMe
O
8a
3.00
1.99
6.09
f1 (ppm)

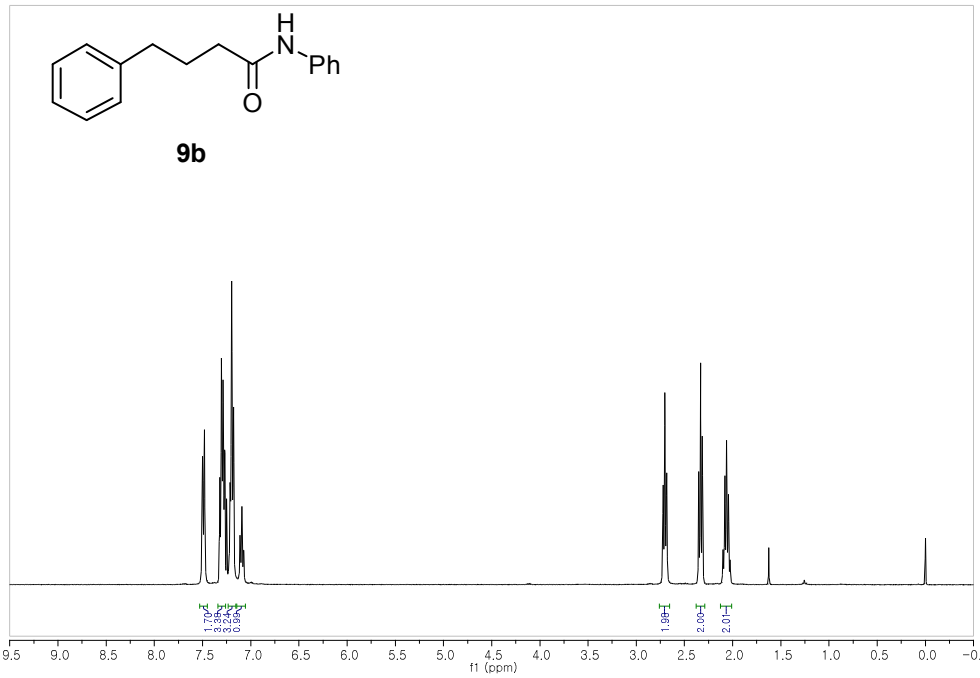

173.82
77.55
77.23
76.91
51.55
42.20
35.10
33.25
26.24
26.35
f1 (ppm)

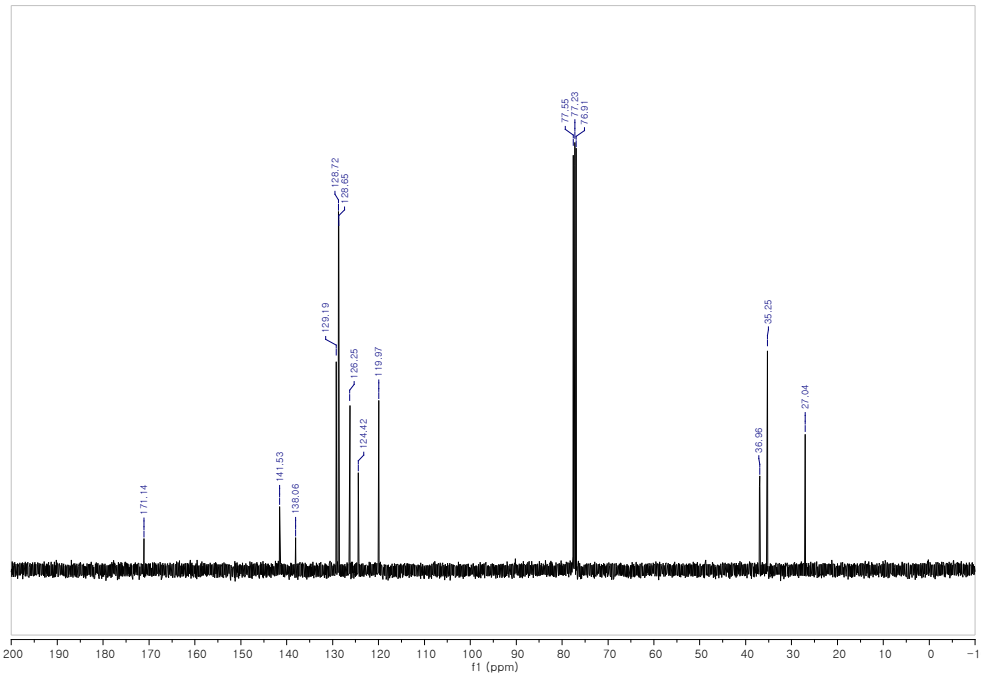

H
N
Ph
O
8b
2.79
2.01
0.99
2.00
6.23
2.14
1.14
1.95
f1 (ppm)

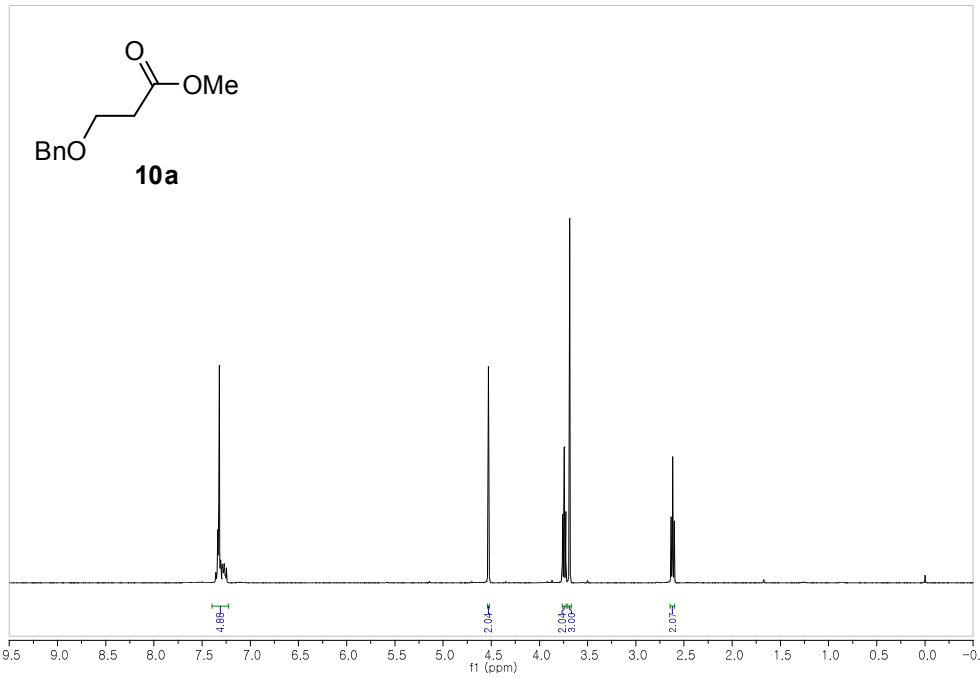

171.19
138.20
129.14
124.37
120.10
77.58
77.26
76.94
46.09
35.73
33.36
26.27
26.39
f1 (ppm)

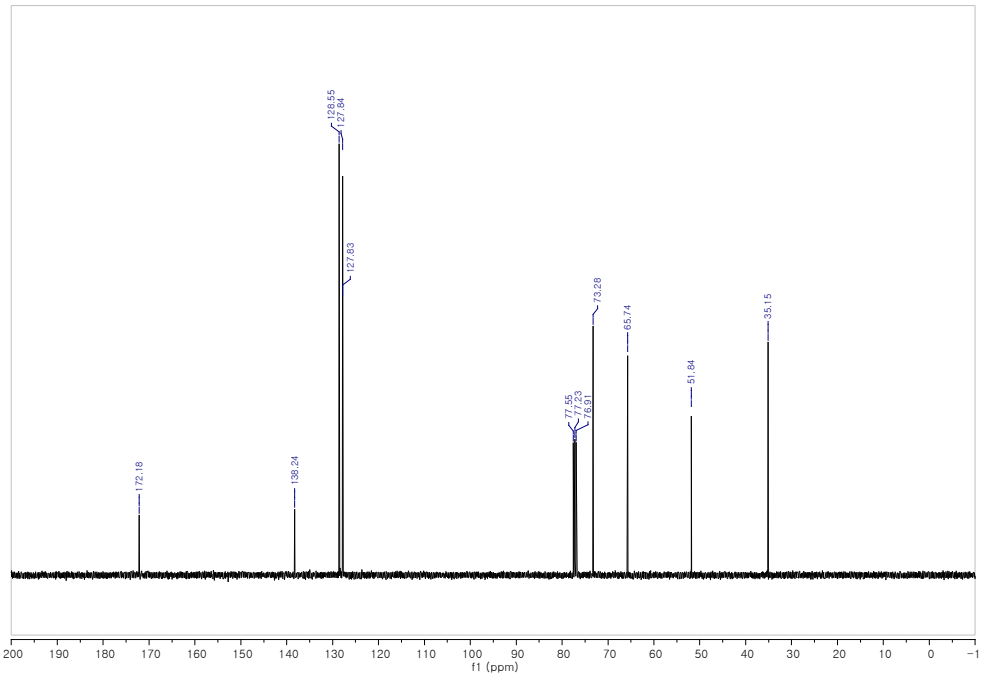

OMe
O
9a
1.87
2.82
3.00
2.11
2.09
2.14
f1 (ppm)

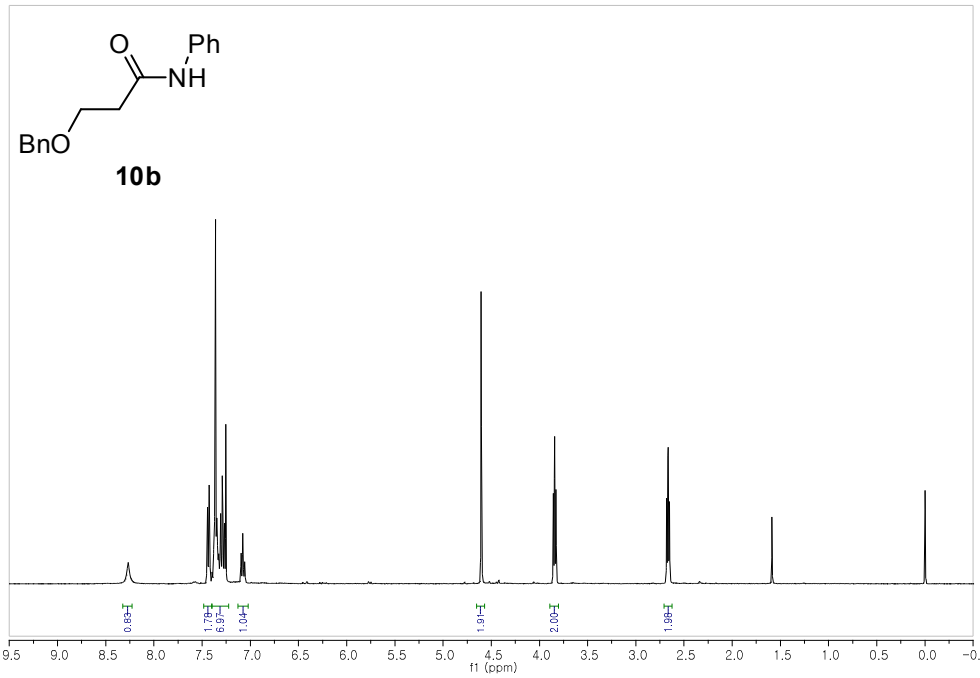

174.08
141.52
128.54
126.14
77.55
77.23
76.91
51.66
35.28
33.54
26.65
f1 (ppm)

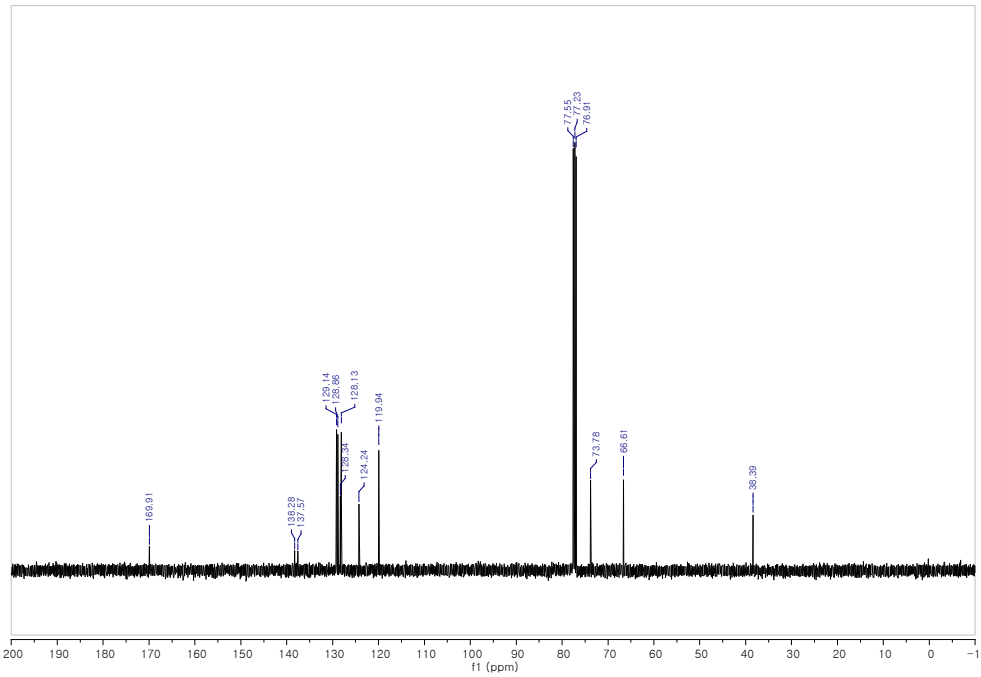

H
N
Ph
O
9b
1.79
1.86
3.24
0.99
1.98
2.00
2.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.
f1 (ppm)

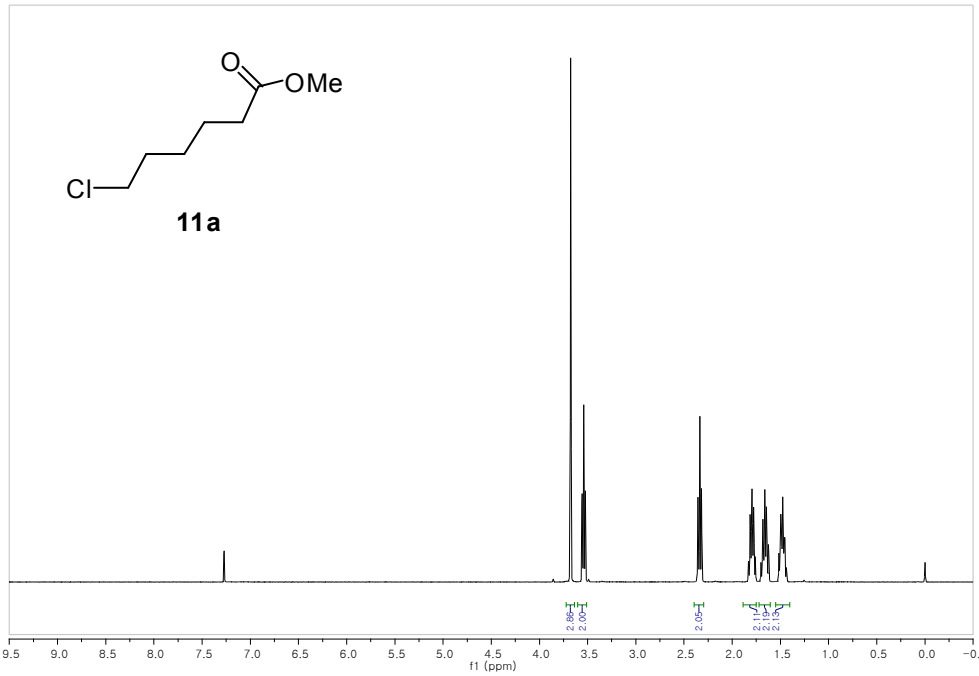

171.14
141.53
138.06
129.19
128.72
128.65
126.25
124.42
119.97
77.55
77.23
76.91
36.25
36.96
27.04
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1(
f1 (ppm)

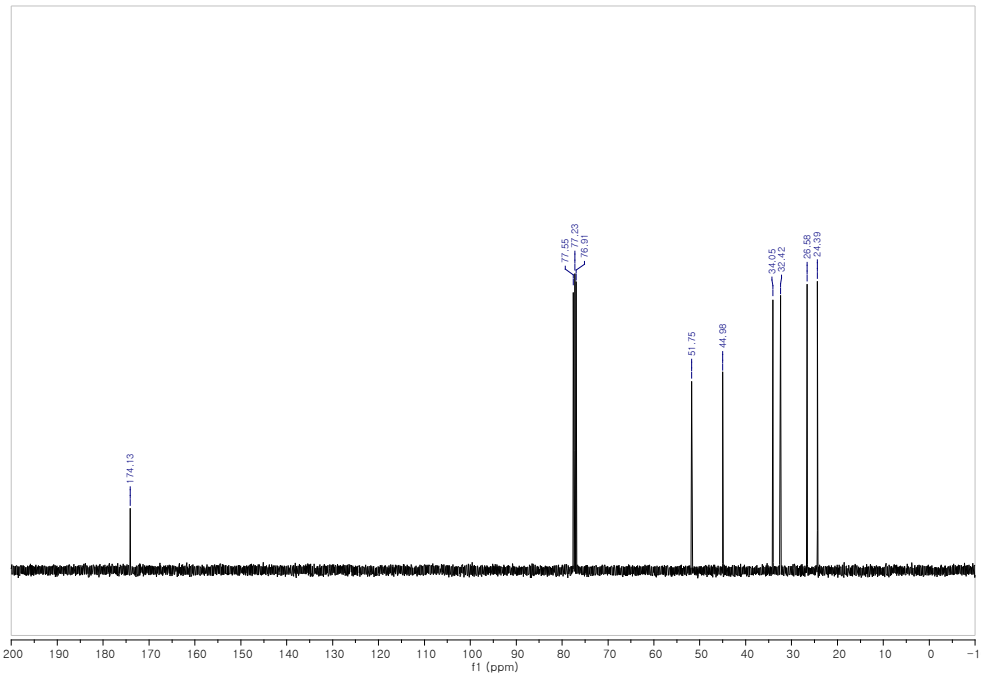

O
OMe
BnO
10a
4.86
2.04
2.04
3.00
2.07
f1 (ppm)

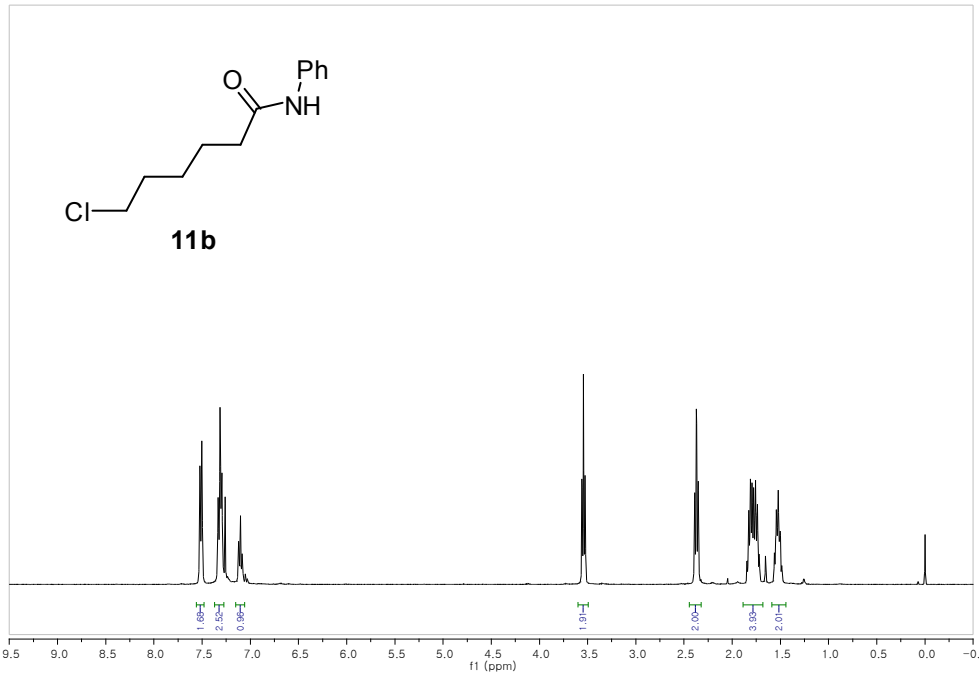

128.55
127.84
127.83
73.28
65.74
51.84
35.15
77.65
77.23
76.91
172.18
138.24
f1 (ppm)

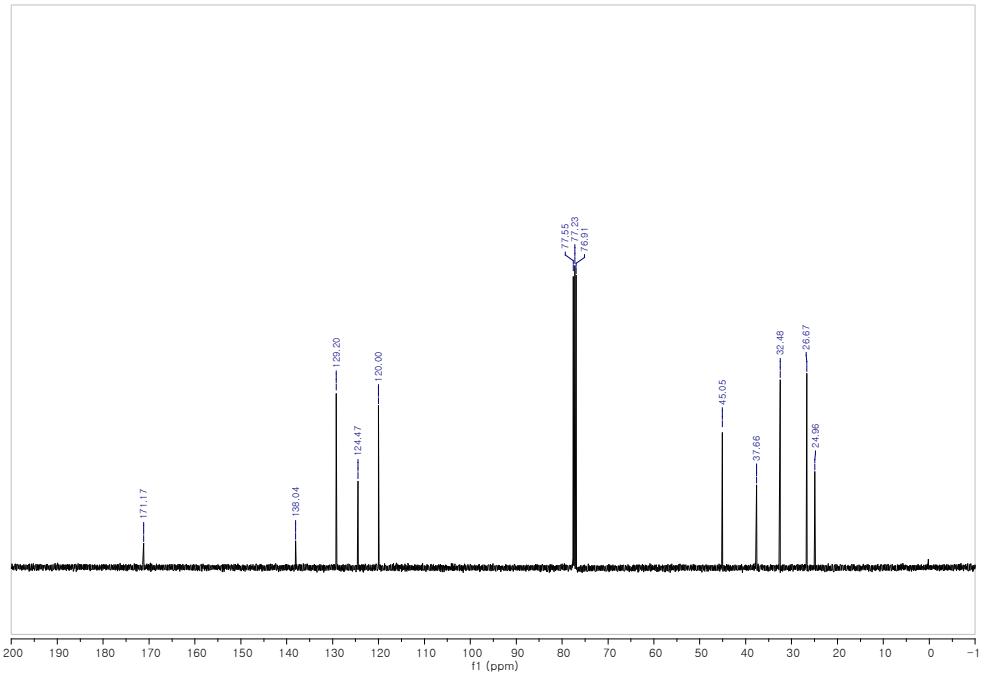

O
Ph
NH
BnO
10b
0.89
1.78
6.97
1.04
1.91
2.00
1.96
f1 (ppm)

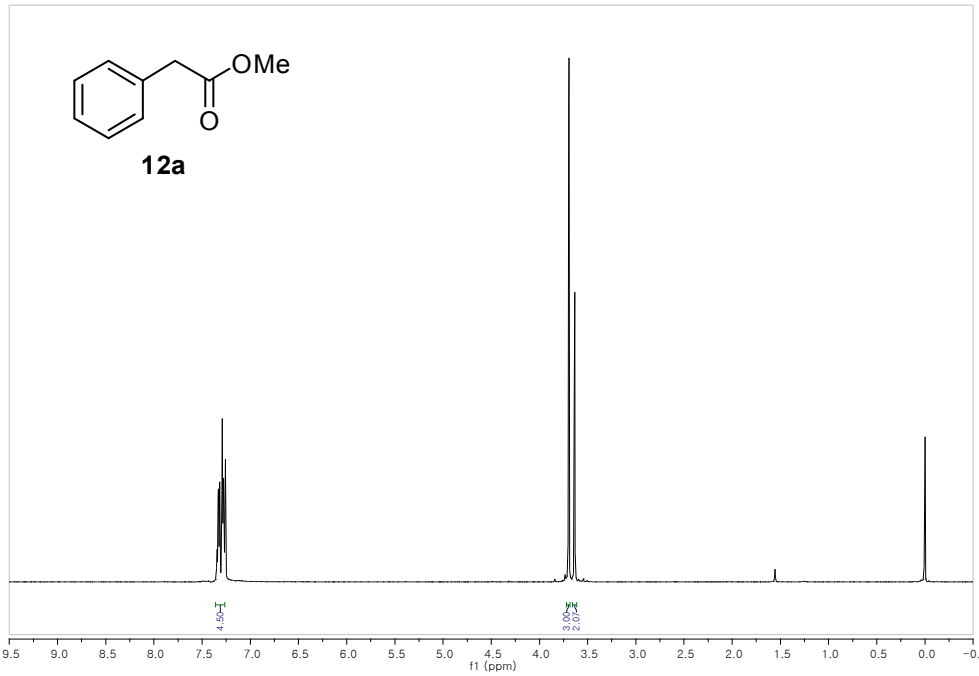

169.91
139.28
137.57
129.14
128.86
128.13
125.34
124.24
119.94
77.55
77.23
76.91
73.76
66.61
38.39
f1 (ppm)

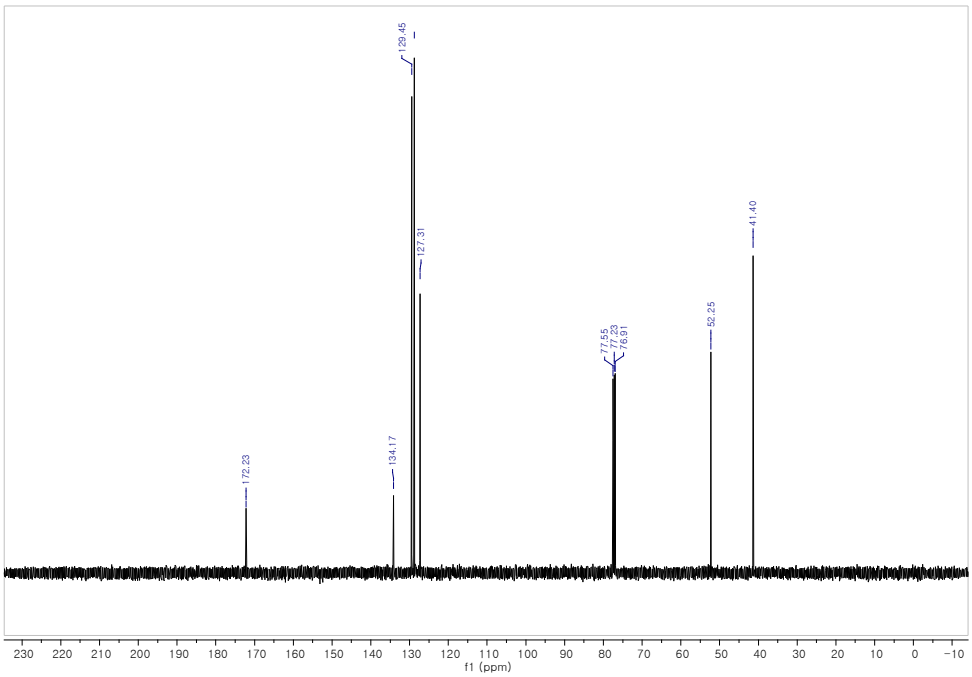

O
OMe
Cl
11a
2.86
2.00
2.05
2.11
2.15
2.15
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

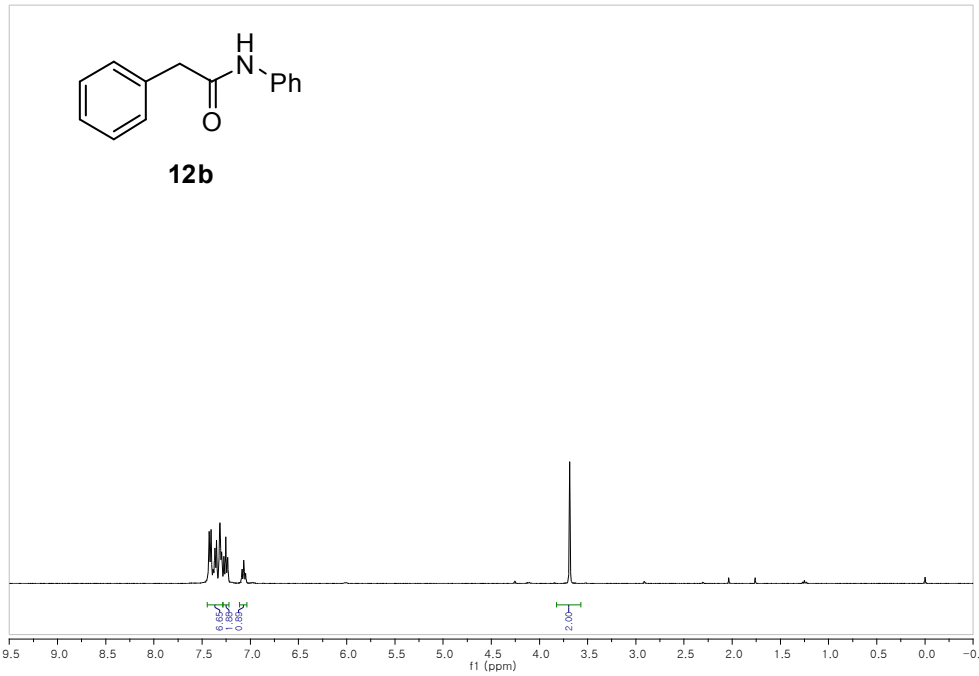

174.13
77.55
77.23
76.91
51.75
44.98
34.05
32.42
26.58
24.39
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

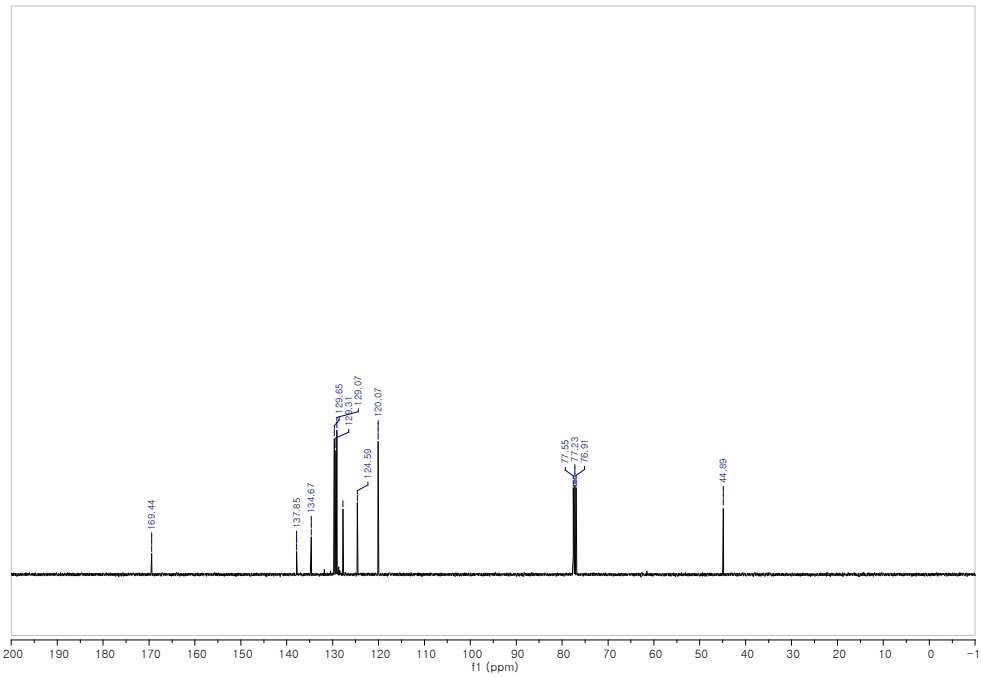

O
Ph
NH
Cl
11b
1.69
2.55
0.96
1.91
2.00
3.95
2.01
f1 (ppm)


77.55
77.23
76.91
129.20
120.00
124.47
138.04
171.17
45.05
37.66
32.48
26.67
24.96
f1 (ppm)


OMe
O
12a
4.90
3.00
2.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


129.45
127.31
77.55
77.23
76.91
52.25
41.40
134.17
172.23
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


H
N
Ph
O
12b
6.66
1.84
0.85
2.00
f1 (ppm)


169.44
137.85
134.67
129.65
129.31
125.07
124.59
120.07
77.55
77.23
76.91
44.89
f1 (ppm)